Chemotherapy Protocols 2020

Current Protocols and "Targeted Therapies"

Klinikum Wels-Grieskirchen, Austria Department of Internal Medicine IV Chairman: J. Thaler, MD, Professor
Vice-Chairman: T. Kühr, MD, Associate Professor

Public General Hospital St. Vinzenz Ltd. Zams, Austria
Department of Internal Medicine
Chairman: E. Wöll, MD, Associate Professor

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Responsible for the content: T. Kühr, E. Wöll, J. Thaler
Layout and design: Dr. Eugen Preuß, ©pdl 2020

Contact:
email: support@chemoprotocols.eu
thomas.kuehr@klinikum-wegr.at e.woell@krankenhaus-zams.at
josef.thaler@klinikum-wegr.at
Phone +43 7242 415 3451 Phone +43 5442 600 7421

PREFACE to the 20th EDITION

We would like to express our thanks for the overwhelming positive response to the previous editions of this handy reference work.

Because of rapid advancements in the areas of hematology and oncology, every year a considerably large number of new therapy protocols are added to those in existence. In order to maintain the size of this book, special attention has been paid to those chemotherapy protocols that are frequently used in the daily routine.

Information on the number of cycles in the oncological protocols should be considered as orientation help; as far as hematological protocols are concerned, in view of even greater diversity in this field, information on cycles has been completely dispensed with.

The therapeutic protocol was developed in cooperation with Mrs. Petra Söllinger MSc (pharmacy sciences). The stability of the effective compounds in the published concentrations was verified.

This book cannot take the place of the major text books in oncology and it is stressed that the indication to therapy and the actual administration of oncologic agents shall remain in the hands of experienced hematologists and oncologists.

We shall also be very grateful to receive feedbacks on this edition in the future.

Wels and Zams, January 2020

Thomas Kuehr, MD, Vice head
Josef Thaler, MD, Head of Department
Ewald Woell, MD, Head of Department

PREFACE to the 1st EDITION

The aim of this book is to present the most important and commonly used chemotherapy protocols in the treatment of solid tumors together with the mode of administration of the drugs and accompanying medication.

Special attention was directed towards designing the contents of this book in such a way as to meet the requirements of the Innsbruck University Clinics regarding preparation of cytostatic medications. In this context we would like to express our thanks to Dr. Elisabeth Semenitz (Hospital Pharmacy, Innsbruck University Clinics) for her valuable support in setting up guidelines for chemotherapy.

In this list, only those tumour entities are referred to which are treated in large numbers in our department.

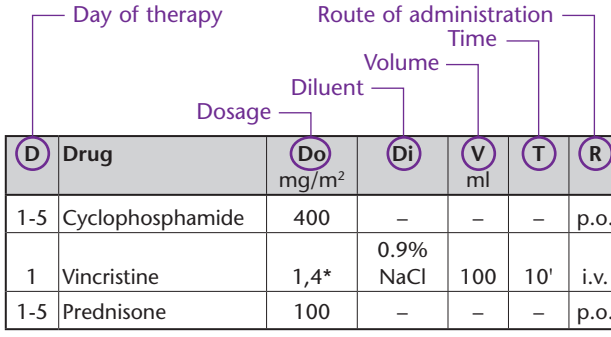
Tumors that are treated very infrequently in our department, or those treated mostly by other clinics could not be addressed in this book. In the appendix, we address briefly the issues of anti-emetic therapy, measures for dealing with extravasation and current study protocols in our department. We plan to regularly issue newer editions and updates of this book; in this connection we request the reader for critical feedback and suggestions.

It should be clear that this book is not a substitute for detailed textbooks on oncology; we draw attention to the fact that decisions regarding indications and administration of drugs should be made only by experienced oncologists.

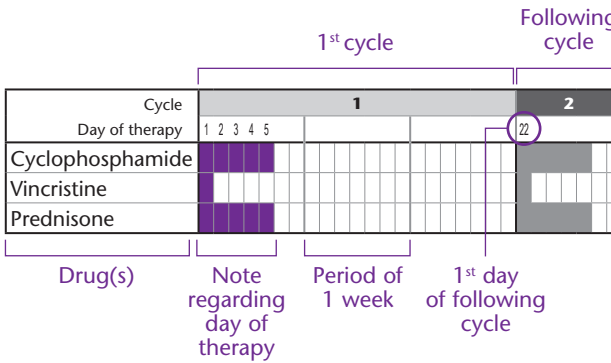
Innsbruck, April 2000

Ewald Woell, MD, Associate Professor, Senior Consultant
Thomas Kuehr, MD, Consultant
Josef Thaler, MD, Associate Professor, Senior Consultant

Key to the symbols used



D	Drug	Do mg/m²	Di	V ml	T	R
1-5	Cyclophosphamide	400	–	–	–	p.o.
1	Vincristine	1,4*	0.9% NaCl	100	10'	i.v.
1-5	Prednisone	100	–	–	–	p.o.



Chemotherapy should be administered in the given sequence.

The MEL Code is given beside the chemotherapy title.

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A Hematology

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B Oncology

A Hematology

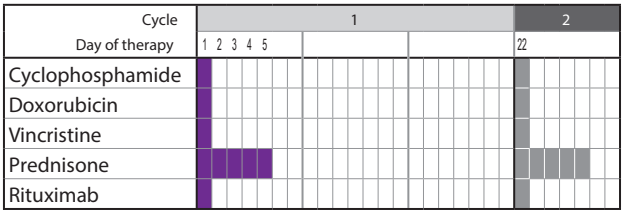
Chapter 1

High Grade NHL

1 High Grade NHL

1.1 CHOP + RITUXIMAB XC264 + XA090

D	Drug	Do mg/m²	Di	V ml	T	R
1	Cyclophosphamide	750	0.9% NaCl	500	1h	i.v.
1	Doxorubicin	50	0.9% NaCl	250	1h	i.v.
1	Vincristine	1.4*	0.9% NaCl	100	10'	i.v.
1-5	Prednisone	40	–	–	–	p.o.
1	Rituximab	375	0.9% NaCl	500	5h (3h)	i.v.



Repetition: Day 22

Note:

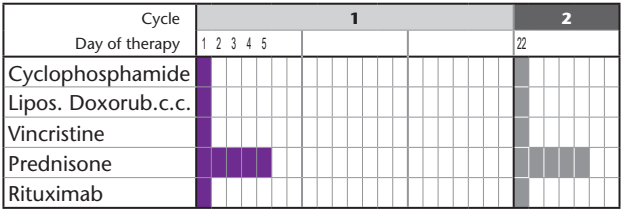
- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg Diphenhydramine is recommended.
- (*) Vincristine max. 2 mg
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative doses ≥500 mg/m^2
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide.

Literature:

Coiffier B. et al., N Engl J Med 346: 235ff, 2002

1.2 COMP + RITUXIMAB *XC346 + XA090*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Cyclophosphamide	750	0.9% NaCl	500	1h	i.v.
1	Liposomal Doxorubicin citrate complex (Myocet®)	50	0.9% NaCl	100	1h	i.v.
1	Vincristine	1.4*	0.9% NaCl	100	10'	i.v.
1-5	Prednisone	40	–	–	–	p.o.
1	Rituximab	375	0.9% NaCl	500	5h (3h)	i.v.



Repetition: Day 22

Number of cycles: 8

Note:

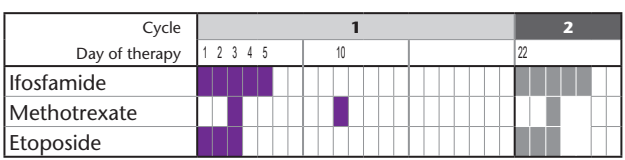
- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h Premedication with 30 mg Diphenhydramine is recommended.
- Liposomal Doxorubicin citrate complex should be dissolved at 0.4 - 1.2 mg/ml
- (*) Vincristine max. 2 mg
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide.

Literature:

Luminari S. et al., Ann Oncol 21: 1492ff, 2010

1.3 IMVP-16 *XC656*

D	Drug	Do mg/m²	Di	V ml	T	R
1-5	Ifosfamide	1000	0.9% NaCl	500	1h	i.v.
3,10	Methotrexate	30	0.9% NaCl	100	15'	i.v.
1-3	Etoposide	100	0.9% NaCl	500	2h	i.v.



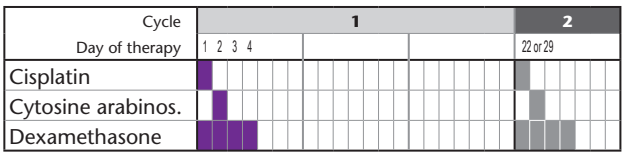
Repetition: Day 22

Note:
- Etoposide should be dissolved in 1000 ml 0.9% NaCl if total dose is ≥ 200 mg
- *Mesna:* Dose is equal to 100% of the Ifosfamide dose, given as 20% of the Ifosfamide dose i.v. at hour 0, followed by 40% of the Ifosfamide dose given orally 2- and 6 hours after start of Ifosfamide.

Literature:
Cabanillas F. et al., Blood 60: 693ff, 1982

1.4 DHAP *XC408*

D	Drug	Do	Di	V ml	T	R
1	Cisplatin	100 mg/m²	0.9% NaCl	1000	24h	i.v.
2	Cytosine arabinoside	2x 2000 mg/m²	0.9% NaCl	2x 500	3h q12h	i.v.
1-4	Dexamethasone	40 mg (absolute)	–	–	–	p.o.



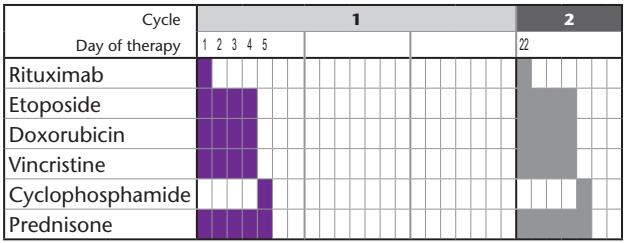
Repetition: Day 22 or 29

Note:
- Cytosine arabinoside: Dose of 1000 mg/m² in patients >70 years of age
- Dexamethasone: Oral administration or as i.v. infusion over 15 min
- Cisplatin (only if GFR ≥60 ml/min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature: Velasquez W. et al., Blood 71: 117ff, 1988

1.5 Dose-adjusted EPOCH-24R *XC492 + XA090*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Rituximab	375	0.9% NaCl	500	5h (3h)	i.v.
1-4	Etoposide*	50	0.9% NaCl	500	24h	i.v.
1-4	Doxorubicin*	10	0.9% NaCl	500	24h	i.v.
1-4	Vincristine*	0.4	0.9% NaCl	500	24h	i.v.
5	Cyclophosphamide	750	0.9% NaCl	500	2h	i.v.
1-5	Prednisone	120#	–	–	–	p.o.



Repetition: Day 22

Number of cycles: 6

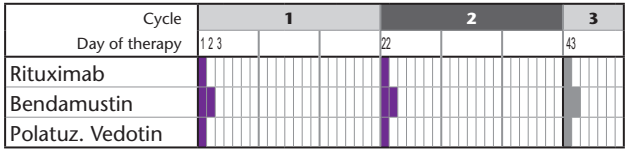
Note:

- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg diphenhydramine is recommended.
- (*) Etoposide, Doxorubicin and Vincristine are admixed together in 0.9% NaCl. The diluent volume will be based on the Etoposide dose for a 24 hour treatment: if ≤ 150 mg/24h = 500 ml, if ≥150 mg/24h = 1000 ml
- (#) Prednisone 120 mg/m^2 divided into two equal doses, administered in the morning and evening.
- G-CSF on day 6 through ANC > 5000 cells/µl past the nadir (measurement of ANC and platelet nadir are based on twice weekly CBC only)
- Dose adjustments: Nadir ANC ≥ 0.5 G/L: 20% increase in Etoposide, Doxorubicin, Cyclophosphamide, Nadir ANC < 0.5 G/L: same dose(s) as last cycle, Nadir ANC <0.5 G/L on at least three measurements or thrombocytes < 25 G/L: 20% decrease in Etoposide, Doxorubicin, Cyclophosphamide.
- Dose adjustments above starting dose level (level 1) apply to Etoposide, Doxorubicin and Cyclophosphamide. Dose adjustments below starting dose level (level 1) apply to Cyclophosphamide only.
- Mesna: 20% of the Cyclophosphamide dose at the time of Cyclophosphamide administration (i.v.), 40% of the Cyclophosphamide dose 2h and 6h after Cyclophosphamide administration (p.o)
- Pneumocytis prophylaxis recommended

Literature: Wilson W. et al., Blood 99: 2685ff, 2002; Dunleavy K. et al., N Engl J Med 368: 1408ff, 2013 Dunleavy K. et al., Lancet Haematol 5: e609ff, 2018

1.6 RITUXIMAB / BENDAMUSTINE / POLATUZUMAB VEDOTIN *XC153 + XA090*

D	Drug	Do	Di	V ml	T	R
1	Rituximab	375 mg/m²	0.9% NaCl	500	5h (3h)	i.v.
1,2	Bendamustine	90 mg/m²	0.9% NaCl	500	30'	i.v.
1	Polatuzumab Vedotin	1.8 mg/kg	0.9% NaCl	100	90'	i.v.



Repetition: Number of cycles: 6 Day 22

Note:

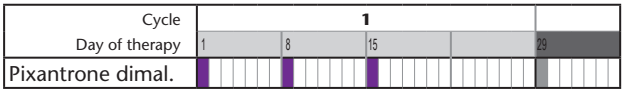
- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg diphenhydramine is recommended.
- Polatuzumab Vedotin at initial administration over 90 min. If well tolerated, subsequent doses can be administered over 30 min.

- Polatuzumab Vedotin should be dissolved at 0.72 – 2.7 mg/ml
- Pneumocystis prophylaxis recommended

Literature:
Sehn H. et al., J Clin Oncol 2019
(DOI: https://doi.org/10.1200/JCO.19.00172)

1.7 PIXANTRONE *XC802*

D	Drug	Do	Di	V	T	R
		mg/m²		ml		
1,8, 15	Pixantrone dimaleate	85*	0.9% NaCl	250	1h	i.v.



Repetition: Day 29

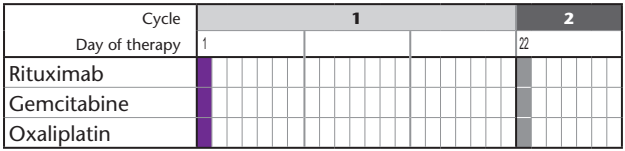
Note:
- (*) Dose equivalent to 50 mg/m² of Pixantrone in its base form

Literature:
Pettengell R. et al., Lancet Oncol 13: 696ff, 2012

1.8 RITUXIMAB / GEMCITABINE / OXALIPLATIN

XA090 + XC604

D	Drug	Do mg/m²	Di	V ml	T	R
1	Rituximab	375	0.9% NaCl	500	5h (3h)	i.v.
1	Gemcitabine	1000	0.9% NaCl	500	30'	i.v.
1	Oxaliplatin	100	5% Glucose	1000	2h	i.v.



Repetition: Day 22
Number of cycles: 6
Note:

- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg Diphenhydramine is recommended.

Literature: Lopez A. et al., Eur J Haematol 80: 127ff, 2007
El Gnaoui T. et al., Ann Oncol 18: 1363ff, 2007

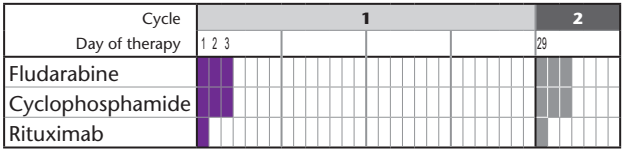
Chapter 2

Low Grade NHL

2 Low Grade NHL

2.1 FLUDARABINE / CYCLOPHOSPHAMIDE / RITUXIMAB *XC528 + XA090*

D	Drug	Do mg/m²	Di	V ml	T	R
1-3	Fludarabine	25	0.9% NaCl	250	30'	i.v.
1-3	Cyclophosphamide	250	0.9% NaCl	500	30'	i.v.
1	Rituximab	500*	0.9% NaCl	500	5h (3h)	i.v.



Repetition: Day 29

Note:

- (*) Rituximab at a dose of 375 mg/m² on day 0 of the first course, and 500 mg/m² on day 1 of the second to sixth courses.
- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 min. intervals, to a maximum of 400 mg/h. Premedication w ith 30 mg Diphenhydramine is recommended.

- *Caution:* Tumor lysis syndrome and protracted T-cell depletion.
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide

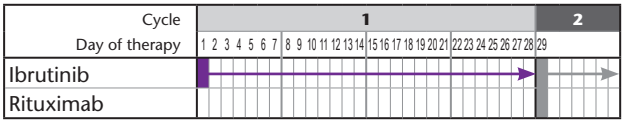
Literature:

Hallek M. et al., Lancet 376: 1164ff, 2010

2.2 IBRUTINIB + RITUXIMAB

XA149 + XA090

D	Drug	Do	Di	V ml	T	R
1-*	Ibrutinib	420 mg	–	–	–	p.o.
1**	Rituximab#	500 mg/m²	0.9% NaCl	500	5h (3h)	i.v.



Repetition: * Continuous administration; until progressive disease or intolerability
Day 29

Number of cycles: 7 (Rituximab)

Note:

- (**) Rituximab: Start will be at cycle 2: day 1: 50 mg/m² i.v., day 2: 325 mg/m² i.v.; cycle 3-7: 500 mg/m² i.v. The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg Diphenhydramine is recommended.

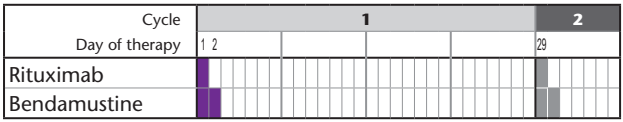
Literature:

Shanafelt T.D. et al., N Engl J Med 381: 432ff, 2019

2.3 BENDAMUSTINE / RITUXIMAB

XC153 + XA090

D	Drug	Do mg/m²	Di	V ml	T	R
1	Rituximab	375	0.9% NaCl	500	5h (3h)	i.v.
1,2	Bendamustine	90	0.9% NaCl	500	30'	i.v.



Repetition: Day 29

Note:

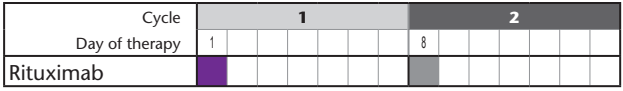
- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg Diphenhydramine is recommended.

Literature:

Rummel M.J. et al., Lancet 381: 1203ff, 2013

2.4 RITUXIMAB *XA090*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Rituximab	375	0.9% NaCl	500	5h (3h)	i.v.



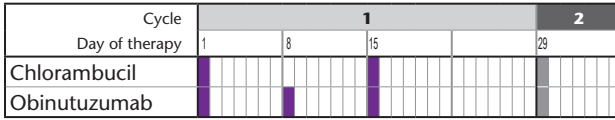
Repetition: Day 8

Note:
- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg Diphenhydramine is recommended.
- A total of **4 cycles** is recommended.

Literature:
Maloney D. et al., Blood 90: 2188ff, 1997

2.5 CHLORAMBUCIL / OBINUTUZUMAB *XA076*

D	Drug	Do	Di	V ml	T	R
1,15	Chlorambucil	0.5 mg/kg	–	–	–	p.o.
1,8, 15	Obinutuzumab*	1000 mg	0.9% NaCl	500	**	i.v.



Repetition: Day 29

Note:

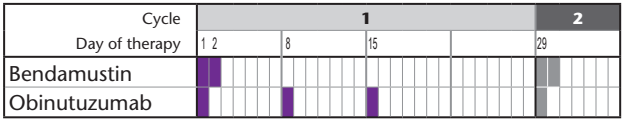
- (*) Obinutuzumab only on day 1 from cycle 2 onward
- (**) Obinutuzumab cycle 1
  - Day 1: 100 mg; administer at 25 mg/h over 4h.
  - Day 2: 900 mg; administer at 50 mg/h; the infusion rate can be escalated in increments of 50 mg/h every 30 to a maximum rate of 400 mg/h.
  - Day 8,15: Infusion can be started at a rate of 100 mg/h and increased by 100mg/h increments every 30 min. to a maximum of 400mg/h.
- Premedication with 30 mg Diphenhydramine recommended

Literature:

Goede V. at al., N Engl J Med 370: 1011ff, 2014

2.6 BENDAMUSTIN / OBINUTUZUMAB *XA076*

D	Drug	Do	Di	V ml	T	R
1,2	Bendamustin	90 mg/m²	0.9% NaCl	500	30'	i.v.
1,8, 15	Obinutuzumab*	1000 mg	0.9% NaCl	500	#	i.v.



Repetition: Day 29

Note:

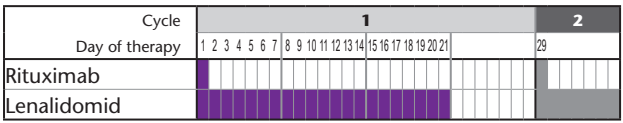
- (*) Obinutuzumab only on day 1 from cycle 2 onwards
- (#) Obinutuzumab cycle 1
  Day 1: 100mg; administer at 25 mg/h over 4h
  Day 2: 900mg; administer at 50 mg/h; the infusion rate can be escalated in increments of 50 mg/h every 30 to a maximum rate of 400 mg/h.
  Day 8,15: Infusion can be started at a rate of 100 mg/h and increased by 100 mg/h increments every 30 min. to a maximum of 400 mg/h.
- Premedication with 30 mg Diphenhydramine recommended
- Obinutuzumab maintenance every 2 months over two years if no evidence of progressive disease is evident
- Obinotuzumab is approved also in combination with CVP or CHOP

Literature:

Marcus R. at al., N Engl J Med 377: 1331ff, 2017
Sehn L.H. et al., Lancet Oncol 17: 1081ff, 2016

2.7 RITUXIMAB / LENALIDOMIDE *XA090*

T	Wirkstoff	D	TL	V ml	Z	A
1*	Rituximab	375 mg/m²	0.9% NaCl	500	5h (3h)	i.v.
1-21	Lenalidomid	20 mg**	–	–	–	p.o.



Repetition: Day 29

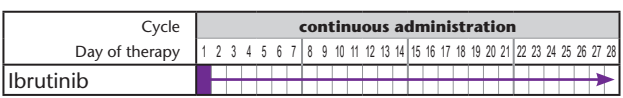
Number of cycles: Rituximab: 5
Lenalidomid: 12

Note:
- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg diphenhydramine is recommended.
- (*) Cycle 1: Rituximab administration d 8, 15, 22 (beginning 1 week after initiation of Lenalidomide)
- (**) Lenalidomide dose 10 mg daily for creatinine clearence 30 to 59 ml/min

Literature:
Leonard J.P. et al.; J Clin Oncol 37: 1188ff, 2019

2.8 IBRUTINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Ibrutinib	420	–	–	–	p.o.



Repetition: * Continuous administration

Note:

- For the treatment of mantle-cell lymphoma the recommended dose is 560 mg/d (4 capsules once daily)
- Ibrutinib can also be administered in combination with Obinutuzumab (Moreno C. et al., Lancet Oncol 20: 43ff, 2019)

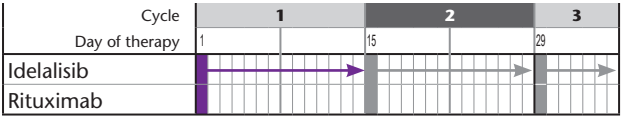
Literature:

Byrd J.C. at al., N Engl J Med 371: 213ff, 2014
Wang M.L. at al., N Engl J Med 369: 507ff, 2013
Woyach J.A. et al., N Engl J Med 379: 2517ff, 2018

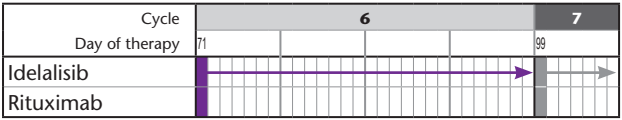
2.9 IDELALISIB / RITUXIMAB *XA149 + XA090*

D	Drug	Do	Di	V ml	T	R
1-*	Idelalisib	300 mg	–	–	–	p.o.
1	Rituximab	375# mg/m²	0.9 NaCl	500	5h (3h)	i.v.

Cycle 1-5:



Cycle 6-8:



Repetition:

* Continuous administration

Rituximab every 2 weeks for 4 doses and then every 4 weeks for 3 doses, for a total of 8 infusions

Note:

- (#) Rituximab 500 mg/m² from cycle 2 onwards
- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h. Subsequent doses can be infused at an initial rate of100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg Diphenhydramine is recommended.

- Premedication with 30 mg Diphenhydramine recommended

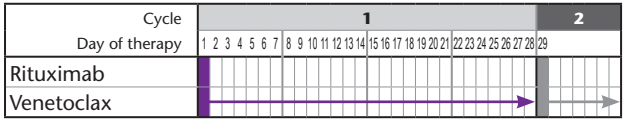
Literature:

Furman R.R. at al., N Engl J Med 370: 997ff, 2014

2.10 VENETOCLAX / RITUXIMAB

XA149 + XA090

D	Drug	Do	Di	V ml	T	R
1	Rituximab	375 mg/m²	0.9% NaCl	500	5 h (3 h)	i.v.
1-*	Venetoclax	400 mg#	–	–	–	p.o.



Repetition: * Continuous administration for 2 years, Rituximab: Day 29

Number of cycles: 6 for Rituximab

Note:

- Rituximab: Start first administration at the end of the venetoclax ramp-up period
  Dose from cycle 2 onwards: 500 mg/m²
  The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h.
  Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h.
  Premedication with 30 mg Diphenhydramine is recommended.

- (#) Venetoclax starting dose: 20 mg d1-7
- Dose increase schedule:

Week	daily dose
1	20 mg
2	50 mg
3	100 mg
4	200 mg
≥5	400 mg

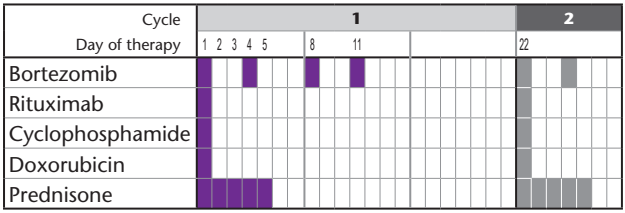
- *Cave:* Venetoclax can cause rapid reduction in tumor, and thus poses a serious risk for tumor lysis syndrome (TLS) in the initial 5-week dose-titration phase. TLS can occur as early as 6 to 8 hours following the first dose of venetoclax and at each dose increase.

Literature:

Seymour J.F. et al., N Engl J Med 378: 1107ff, 2018
Roberts A.W. et al., N Engl J Med 374: 311ff, 2016
Stilgenbauer S. et al., Lancet Oncol 17: 768ff, 2016

2.11 BORTEZOMIB / RITUXIMAB – CYCLOPHOSPHAMIDE / DOXORUBICIN / PREDNISONE *XA020 + XA090*

D	Drug	Do mg/m²	Di	V ml	T	R
1,4, 8,11	Bortezomib	1.3	–	–	–	s.c.
1	Rituximab	375	0.9% NaCl	500	5 h (3 h)	i.v.
1	Cyclophosphamide	750	0.9% NaCl	500	1 h	i.v.
1	Doxorubicin	50	0.9% NaCl	500	1 h	i.v
1-5	Prednisone	100	–	–	–	p.o.



Repetition: Day 22

Number of cycles: 6-8

Note:

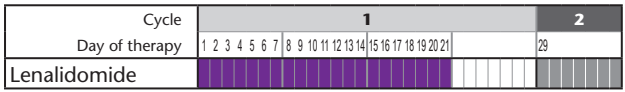
- Rituximab: The first initial rate for infusion is 50 mg/h; after the first 30 minutes, it can be escalated in 50 mg/h increments every 30 minutes, to a maximum of 400mg/h. Subsequent doses can be infused at an initial rate of 100 mg/h, and increased by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h. Premedication with 30 mg Diphenhydramine is recommended.
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative doses ≥ 500 mg/m^2
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide
- Bortezomib concentration at 2.5 mg/ml

Literature:

Robak T. et al., N Engl J Med 372: 944ff, 2015

2.12 LENALIDOMIDE *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-21	Lenalidomide	25	–	–	–	p.o.



Repetition: Day 29

Note:
- Thromboprophylaxis is recommended

Literature:
Trneny M. et al., Lancet Oncol 17: 319ff, 2016

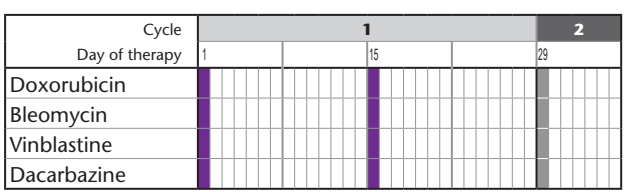
Chapter 3

Hodgkin's Disease

3 Hodgkin's Disease

3.1 ABVD *XC024*

D	Drug	Do mg/m²	Di	V ml	T	R
1,15	Doxorubicin	25	0.9% NaCl	250	1h	i.v.
1,15	Bleomycin	10	–	–	Bolus	i.v.
1,15	Vinblastine	6	0.9% NaCl	100	10'	i.v.
1,15	Dacarbazine	375	0.9% NaCl	500	30'	i.v.



Repetition: Day 29

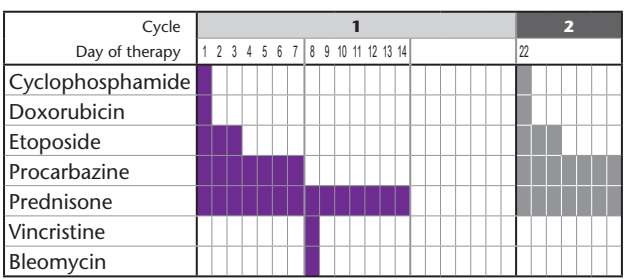
Note:
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative doses ≥500 mg/m²
- Dacarbazine: light-resistant infusion set mandatory

Literature:
Santoro A. et al., Cancer Chemother Pharmacol 2: 101ff, 1979

3.2 BEACOPP (intensified)

XC148 (Day 1-3); XC152 (Day 8)

D	Drug	Do mg/m²	Di	V ml	T	R
1	Cyclophosphamide	1250	0.9% NaCl	500	1h	i.v.
1	Doxorubicin	35	0.9% NaCl	250	1h	i.v.
1-3	Etoposide	200	0.9% NaCl	1000	1h	i.v.
1-7	Procarbazine	100	–	–	–	p.o.
1-14	Prednisone	40	–	–	–	p.o.
8	Vincristine	1.4*	0.9% NaCl	100	10'	i.v.
8	Bleomycin	10	–	–	Bolus	i.v.



Repetition: Day 22

Note:

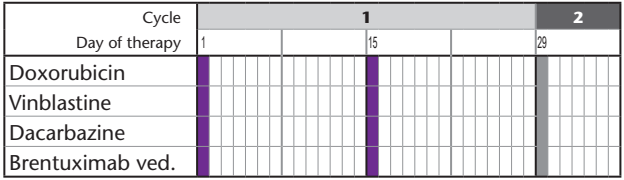
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative doses ≥500 mg/m^2
- Etoposide should be dissolved in 1000 ml 0.9% NaCl if total dose is ≥ 200 mg
- (*) Vincristine max. 2 mg
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide
- G-CSF obligatory on Day 8 until leukocytes >1000/mm^3 is achieved and the nadir is crossed. Continuation of therapy only 48 h after discontinuation of G-CSF
  Dose: 300 µg/d s.c. if bodyweight <75 kg; 450 µg/ kg s.c. if bodyweight >75 kg

Literature:

Diehl V. et al., N Engl J Med 348: 2386ff, 2003

3.3 A + AVD *XA064*

D	Drug	Do	Di	V ml	T	R
1,15	Doxorubicin	25 mg/m²	0.9% NaCl	250	1h	i.v.
1,15	Vinblastine	6 mg/m²	0.9% NaCl	100	10'	i.v.
1,15	Dacarbazine	375 mg/m²	0.9% NaCl	500	30'	i.v.
1,15	Brentuximab vedotin	1.2 mg/kg	0.9% NaCl	250	30'	i.v.



Repetition: Day 29

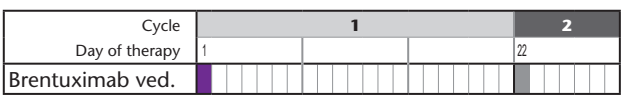
Number of cycles: 6

Note:
- Brentuximab should be dissolved at 0.4 - 1.2 mg/ml
- Brentuximab will be started within approximately 1 hour after completion of AVD.
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative doses ≥500 mg/m²
- Dacarbazine: light-resistant infusion set mandatory

Literature: Connors J.M. et al., N Engl J Med 378: 331ff, 2018

3.4 BRENTUXIMAB *XA064*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Brentuximab vedotin	1.8	0.9% NaCl	250	30'	i.v.



Repetition: Day 22

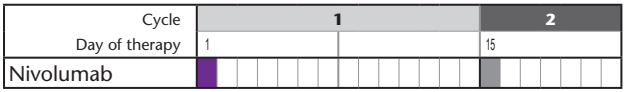
Number of cycles: Up to 8

Note:
- Brentuximab should be dissolved at 0.4 - 1.2 mg/ml

Literature:
Jounes A. et al., J Clin Oncol 30: 2183ff, 2012

3.5 NIVOLUMAB *XA085*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Nivolumab*	3	0.9% NaCl	100	60'	i.v.



Repetition: Day 15

Number of cycles: Until progressive disease or intolerability

Note:
- Nivolumab should be dissolved at 1-10 mg/ml
- (*) Nivolumab can also be administered at 240 mg flat-dose every 2 weeks (Zhao X. et al., Ann Oncol 28: 2002ff, 2017) or at 480 mg every 4 weeks (Long G.V. et al.; Ann Oncol 29: 2208ff, 2018)

Literature:
Younes A. et al., Lancet Oncol 17: 1283ff, 2016

3.6 PEMBROLIZUMAB *XA081*

D	Drug	Do mg	Di	V ml	T	R
1	Pembrolizumab	200	0.9% NaCl	100	60'	i.v.

Cycle	1			2
Day of therapy	1			22
Pembrolizumab				

Repetition: Day 22

Number of cycles: For a maximum of 24 months or until progressive disease or intolerability

Note:
- Pembrolizumab should be dissolved at 1-10 mg/ml

Literature:
Chen R. et al., J Clin Oncol 35: 2125ff, 2017

Chapter 4

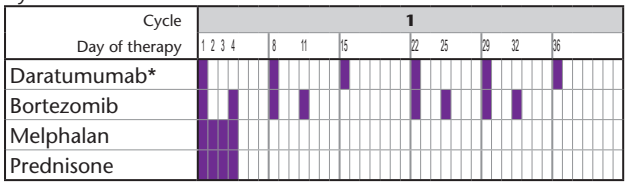
Multiple Myeloma

4 Multiple Myeloma

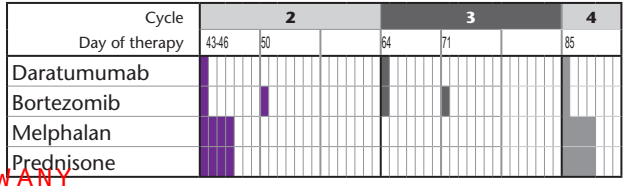
4.1 DARATUMUMAB / BORTEZOMIB / MELPHALAN / PREDNISONE *XA071 + XA020*

D	Drug	Do	Di	V ml	T	R
1*	Daratumumab	16 mg/kg	0.9% NaCl	500	7h (3h)	i.v.
1,8, 22, 29#	Bortezomib	1,3 mg/m²	–	–	–	s.c.
1-4	Melphalan	9 mg/m²	–	–	–	p.o.
1-4	Prednisone	60 mg/m²	–	–	–	p.o.

Cycle 1:



Cycle 2 - 9:



Repetition: Bortezomib/Melphalan/Prednisone: d 43

(#) Bortezomib:
- Cycle 1: twice weekly on weeks 1,2,4,5 (q d43)
- Cycle 2-9: once weekly on weeks 1,2,4,5 (q d43)

(*) Daratumumab:
- Cycle 1: d1,8,15,22,29,36 (q43);
- Cycle 2-9: d1 (q22);
- Cycle 10 onwards: d1 (q29)

Number of cycles: Up to 9

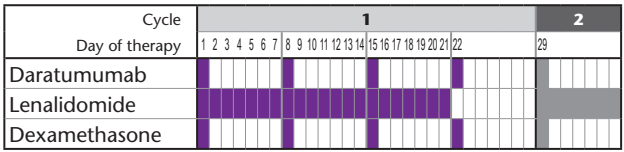
Note:
- Daratumumab: Dilution volume during the 1st infusion: 1000 ml, from the 2nd infusion onwards: 500 ml. The initial rate for the first and second infusion is 50 ml/h; after the first 60 minutes it can be escalated in 50 ml/h increments every 60 minutes, to a maximum of 200 ml/h. Subsequent doses can be infused at an initial rate of 100 ml/h, and increased by 50 ml/h increments at 60 minutes intervals, to a maximum of 200ml/h.
- *Premedication:* 30 mg Diphenhydramine i.v., 12 mg Dexamethasone i.v.; 1000 mg Paracetamol p.o.
- *Postmedication:* 8 mg Dexamethasone (Day 2,3) following the first four infusions. In case of no major IRRs, the post-infusion medication may be discontinued.
- Bortezomib concentration at 2.5 mg/ml

Literature:
Mateos M.-V. et al., N Engl J Med 378: 518ff, 2018

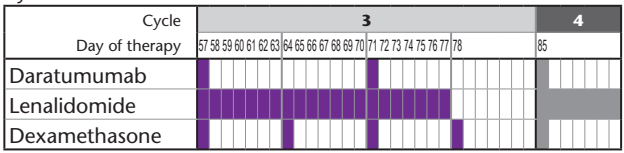
4.2 DARATUMUMAB / LENALIDOMIDE / DEXAMETHASONE XA071

D	Drug	Do	Di	V ml	T	R
1,8, 15, 22*	Daratumumab	16 mg/kg	0.9% NaCl	500#	7h (3h)	i.v.
1-21	Lenalidomide	25 mg	–	–	–	p.o.
1,8, 15, 22	Dexamethasone	40 mg	–	–	–	p.o.

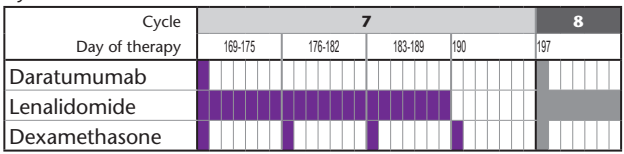
Cycle 1 & 2:



Cycle 3 - 6:



Cycle 7 onwards:



Repetition: Lenalidomide, Dexamethasone: d 29
* Daratumumab:
cycle 1-2: d1,8,15,22 (q29);
cycle 3-6: d1 (q15);
cycle 7 onwards: d1 (q29)

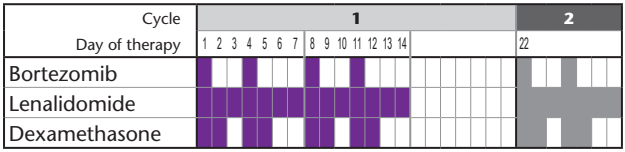
Note:

- (#) Daratumumab: Dilution volume during the 1st infusion: 1000 ml, from the 2nd infusion onwards: 500 ml.
  The initial rate for the first and second infusion is 50 ml/h; after the first 60 minutes it can be escalated in 50 ml/h increments every 60 minutes, to a maximum of 200 ml/h. Subsequent doses can be infused at an initial rate of 100 ml/h, and increased by 50 ml/h increments at 60 minutes intervals, to a maximum of 200 ml/h.
  Premedication: 30 mg Diphenhydramine i.v., 12 mg Dexamethasone i.v.; 1000 mg Paracetamol p.o.
  Postmedication: 8 mg Dexamethasone (Day 2,3) following the first four infusions. In case of no major IRRs, the post-infusion medication may be discontinued.
- Thromboprophylaxis is recommended

Literature:
Dimopoulos M.A. et al., N Engl J Med 375: 1319ff, 2016
Facon et al., N Engl J Med 380: 2104ff, 2019

4.3 BORTEZOMIB / LENALIDOMIDE / DEXAMETHASONE *XA020*

D	Drug	Do	Di	V ml	T	R
1,4, 8,11	Bortezomib	1.3 mg/m²	–	–	–	s.c.
1-14	Lenalidomide	25 mg	–	–	–	p.o.
1,2, 4,5, 8,9 11, 12	Dexamethasone	20 mg	–	–	–	p.o.



Repetition: Day 22
Number of cycles: 8

Note:

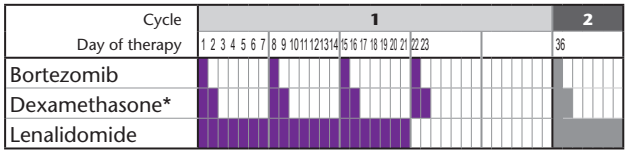
- From cycle 9 onwards: Lenalidomide 25 mg day 1-21 and Dexamethasone 40 mg day 1,8,15,22; Repetition: day 29
- Bortezomb concentration at 2.5 mg/ml
- Thromboprophylaxis is recommended

Literature:
Durie B. et al., Lancet 389: 519ff, 2017

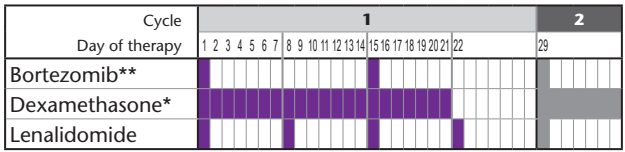
4.4 BORTEZOMIB / LENALIDOMIDE / DEXAMETHASONE – VRD lite *XA020*

D	Drug	Do	Di	V ml	T	R
1,8, 15, 22	Bortezomib**	1.3 mg/m²	–	–	–	s.c.
1,2, 8,9, 15, 16, 22, 23	Dexamethasone*	20 mg	–	–	–	p.o.
1-21	Lenalidomide	15 mg	–	–	–	p.o.

Cycle 1 - 9, Induction:



Cycle 10 - 15, Consolidation:



Repetition: Induction (cycles 1-9): Day 35;
Consolidation (cycles 10-15)**: Day 28

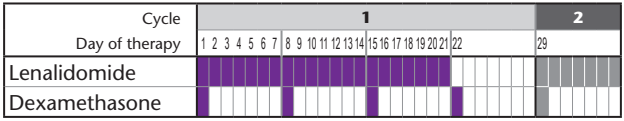
Note:
- Dexamethasone: For patients >75 years of age on days 1, 8, 15, 22
- (**): Consolidation: Bortezomib 1.3 mg/m^2 d1,15, Lenalidomide 15 mg d1-21
- From cycle 16 onwards: Lenalidomide maintenance therapy at the discretion of the treating physician
- Bortezomib concentration at 2.5 mg/ml
- Thromboprophylaxis is recommended

Literature:
O'Donnell E.K. et al., Br. J. Haematol 182: 222ff, 2018

4.5 LENALIDOMIDE / DEXAMETHASONE

XA149

D	Drug	Do mg	Di	V ml	T	R
1-21	Lenalidomide	25	–	–	–	p.o.
1,8, 15, 22	Dexamethasone	40	–	–	–	p.o.



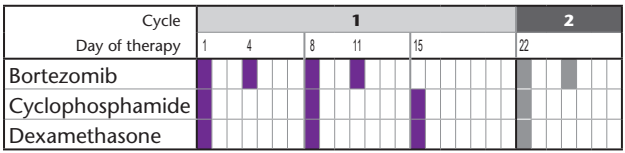
Repetition: Day 29

Note:
- Thromboprophylaxis is recommended

Literature:
Rajkumar S.V., Lancet Oncol 11: 29ff, 2010
Benboubker L. et al., N Engl J Med 371: 906ff, 2014

4.6 BORTEZOMIB / CYCLOPHOSPHAMIDE / DEXAMETHASONE *XA020*

D	Drug	Do	Di	V ml	T	R
1,4, 8,11	Bortezomib	1.3 mg/m²	–	–	–	s.c.
1,8, 15	Cyclophosphamide	500 mg/m²	0.9% NaCl	500	1h	i.v.
1,8 15	Dexamethasone	40 mg	–	–	–	p.o.



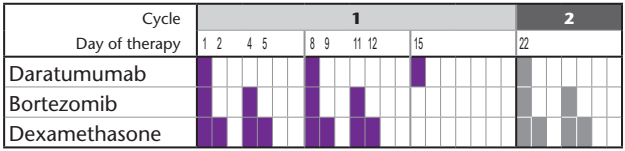
Repetition: Day 22

Note:
- Bortezomib concentration at 2.5 mg/ml
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide

Literature:
Kumar S. et al., Blood 119: 4375ff, 2012

4.7 DARATUMUMAB / BORTEZOMIB / DEXAMETHASONE *XA071 + XA020*

D	Drug	Do	Di	V ml	T	R
1,8, 15*	Daratumumab	16 mg/kg	0.9% NaCl	500	7h (3h)	i.v.
1,4, 8,11	Bortezomib	1.3 mg/m²	–	–	–	s.c.
1,2, 4,5, 8,9 11, 12	Dexamethasone	20 mg	–	–	–	p.o.



Repetition: Bortezomib/Dexamethasone: Day 22
(*) Daratumumab:
Cycle 1-3: d1,8,15 (q22)
Cycle 4-8: d1 (q29)

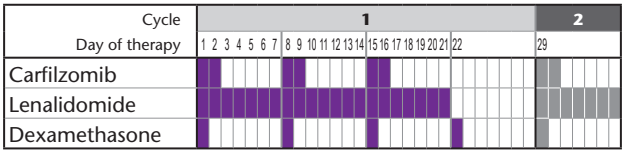
Note:
- Dilution volume during the 1st infusion: 1000 ml, from the 2nd infusion onwards: 500 ml.
- Daratumumab: The initial rate for the first and second infusion is 50ml/h; after the first 60 minutes it can be escalated in 50ml/h increments every 60 minutes, to a maximum of 200 ml/h. Subsequent doses can be infused at an initial rate of 100ml/h, and increased by 50 ml/h increments at 60 minutes intervals, to a maximum of 200 ml/h.

- *Premedication:* 30 mg Diphenhydramine i.v., 12 mg Dexamethasone i.v.; 1000 mg Paracetamol p.o.
- *Postmedication:* 8 mg Dexamethasone (Day 2,3) following the first four infusions. In case of no major IRRs, the post-infusion medication may be discontinued.
- Bortezomb concentration at 2.5 mg/ml
- Thromboprophylaxis is recommended.

Literature:
Palumbo A. et al., N Engl J Med 375: 754ff, 2016

4.8 CARFILZOMIB / LENALIDOMIDE / DEXAMETHASONE *XA022*

D	Drug	Do	Di	V ml	T	R
1,2, 8,9, 15, 16	Carfilzomib	20* mg/m²	5% Glucose	100	30'	i.v.
1-21	Lenalidomide	25 mg	–	–	–	p.o.
1,8, 15, 22	Dexamethasone	40 mg	–	–	–	p.o.



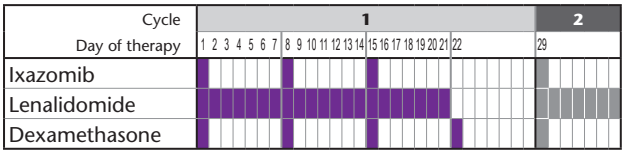
Repetition: Day 29

Note:
- (*) Carfilzomib is administered at a starting dose of 20 mg/m² in cycle 1 on days 1 and 2. If tolerated, the dose should be increased to 27 mg/m² on day 8 of cycle 1.
- Adequate hydration is required before dose administration in cycle 1, especially in patients at high risk of tumor lysis syndrome or renal toxicity.
- Thromboprophylaxis is recommended

Literature:
Stewart A.K. et al., N Engl J Med 372: 142ff, 2015

4.9 IXAZOMIB / LENALIDOMIDE / DEXAMETHASONE *XA149*

T	Wirkstoff	D mg	TL	V ml	Z	A
1,8, 15	Ixazomib	4	–	–	–	p.o.
1-21	Lenalidomide	25	–	–	–	p.o.
1,8, 15, 22	Dexamethasone	40	–	–	–	p.o.



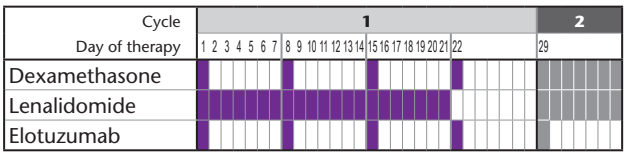
Repetition: Day 29

Note:
- Thromboprophylaxis is recommended

Literature:
Moreau P. et al., N Engl J Med 374: 1621ff, 2016

4.10 ELOTUZUMAB / LENALIDOMIDE / DEXAMETHASONE *XA972*

D	Drug	Do	Di	V ml	T	R
1,8, 15, 22	Dexamethasone	36 mg[#]	–	–	–	p.o.
1-21	Lenalidomide	25 mg	–	–	–	p.o.
1,8, 15, 22*	Elotuzumab	10 mg/kg	0.9% NaCl	230	–	i.v.



Repetition: Day 29

Note:

- (*) From cycle 3 onwards: Elotuzumab d1, 15
- (#) Dexamethasone: 28 mg p.o. 3-24h before Elotuzumab, 8 mg i.v. 45-90 minutes prior to Elotuzumab
- From cycle 3 onwards: 40 mg p.o. d8, 22; 28 mg + 8 mg d1,15
- Elotuzumab: The administration in cycle 1, dose 1 must be initiated at an infusion rate of 0.5 ml/min. If the infusion is well tolerated the infusion rate may be increased to 1 ml/min after 30-60 minutes. It can be further escalated to 2 ml/min. The administration in cycle 1, dose 2 may be initiated at an infusion rate of 3 ml/min. If the infusion is well tolerated the infusion rate may be increased to 4 ml/min after 30 minutes.

The administration in cycle 1, dose 3 and 4 may be initiated at an infusion rate of 5 ml/min. The maximum infusion rate should not exceed 5 ml/min.

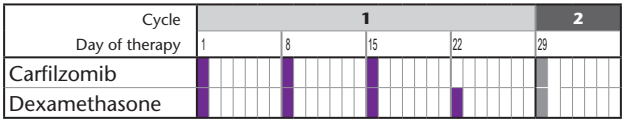
- Premedication: 30 mg Diphenhydramine i.v., Famotidine 20 mg p.o.; 1000 mg Paracetamol p.o.

Literature:

Lonial S. et al., N Engl J Med 373: 621ff, 2015

4.11 CARFILZOMIB / DEXAMETHASONE
XA022

D	Drug	Do	Di	V ml	T	R
1, 8, 15	Carfilzomib	70* mg/m²	5% Glucose	100	30'	i.v.
1, 8, 15, 22#	Dexamethasone	40 mg	–	–	–	p.o.



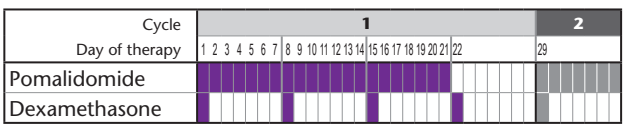
Repetition: Day 29

Note:
- (*) Carfilzomib cycle 1, day 1: 20 mg/m²; thereafter 70 mg/m².
- (#) Dexamethasone at 40 mg on days 1,8,15 (all cycles) and 22 (cycles 1-9 only)
- Adequate hydration is required before dose administration in cycle 1, especially in patients at high risk of tumor lysis syndrome or renal toxicity.

Literature:
Moreau P. et al., Lancet Oncol 19: 953ff, 2018

4.12 POMALIDOMIDE / DEXAMETHASONE
XA149

D	Drug	Do mg	Di	V ml	T	R
1-21	Pomalidomide	4	–	–	–	p.o.
1,8, 15, 22	Dexamethasone	40	–	–	–	p.o.



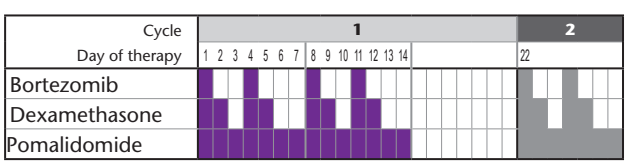
Repetition: Day 29

Note:
- Thromboprophylaxis is recommended

Literature:
San-Miguel J.F. et al., Lancet Oncol 14: 1055ff, 2013

4.13 POMALIDOMIDE / BORTEZOMIB / DEXAMETHASONE *XA020*

D	Drug	Do mg	Di	V ml	T	R
1,4, 8, 11*	Bortezomib	1.3 mg/m²	–	–	–	s.c.
1,2, 4,5, 8,9, 11, 12	Dexamethasone	20 mg	–	–	–	p.o.
1-14	Pomalidomide	4 mg	–	–	–	p.o.



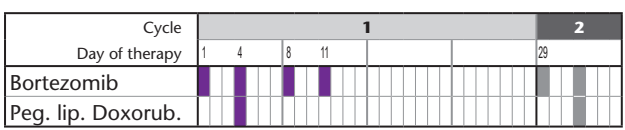
Repetition: Day 22

Note:
- (*) Bortezomib, Dexamethasone: from cycle 9 onwards: d1,8 (q22)
- Bortezomib concentration at 2.5 mg/ml
- Thromboprophylaxis is recommended

Literature:
Richardson et al., Lancet Oncol. 20: 781ff; 2019

4.14 PEGYLATED LIPOSOMAL DOXORUBICIN / BORTEZOMIB *XC452 + XA020*

D	Drug	Do mg/m²	Di	V ml	T	R
1,4, 8,11	Bortezomib	1.3	–	–	–	s.c.
4	Pegylated liposomal Doxorubicin (Caelyx®)	30	5% Glucose	250	1h	i.v.



Repetition: Day 29

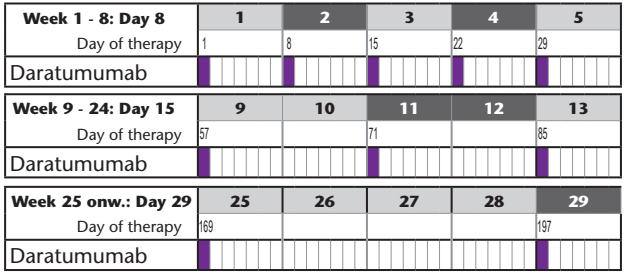
Number of cycles: 8

Note:
- Pegylated liposomal Doxorubicin should be dissolved in 500 ml of 5% Glucose in case the total dose exceeds 90 mg.
- Bortezomib concentration at 2.5 mg/ml

Literature:
Orlowski R.Z. et al., J Clin Oncol 25: 3892ff, 2007
Moreau P. et al., Lancet Oncol 12: 431ff, 2011

4.15 DARATUMUMAB *XA071*

D	Drug	Do mg/kg	Di	V ml	T	R
1*	Daratumumab	16	0.9% NaCl	500	7h (3)	i.v.



Repetition:
* week 1 - 8: d8
* week 9-24: d15
* week 25 onwards: d29

Note:
- Dilution volume during the 1st infusion: 1000 ml, from the 2nd infusion onwards: 500 ml.
- Daratumumab: The initial rate for the first and second infusion is 50ml/h; after the first 60 minutes it can be escalated in 50ml/h increments every 60 minutes, to a maximum of 200 ml/h. Subsequent doses can be infused at an initial rate of 100ml/h, and increased by 50 ml/h increments at 60 minutes intervals, to a maximum of 200ml/h.
- *Premedication:* 30 mg Diphenhydramine i.v., 12 mg Dexamethasone i.v.; 1000 mg Paracetamol p.o.
- *Postmedication:* 8 mg Dexamethasone (d2,3) following the first four infusions. In case of no major IRRs, the post-infusion medication may be discontinued.

Literature: Lonial S. et al., Lancet 387: 1551ff, 2016

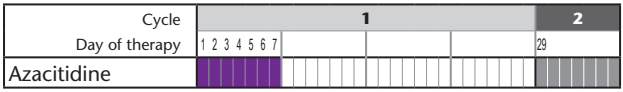
Chapter 5

Myelodysplastic Syndrome

5 Myelodysplastic Syndrome

5.1 AZACITIDINE *XA025*

D	Drug	Do mg/m²	Di	V ml	T	R
1-7	Azacitidine	75	–	–	–	s.c.

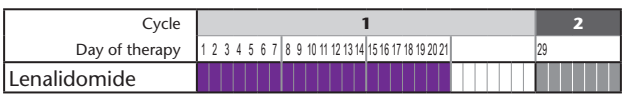


Repetition: Day 29

Literature:
Silverman L.R. et al., J Clin Oncol 20: 2429ff, 2002

5.2 LENALIDOMIDE *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-21	Lenalidomide	10	–	–	–	p.o.



Repetition: Day 29

Note:
- For the treamtent of patients with transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality.
- Thromboprophylaxis is recommended

Literature:
Fenaux P. et al., Blood 118: 3765ff, 2011

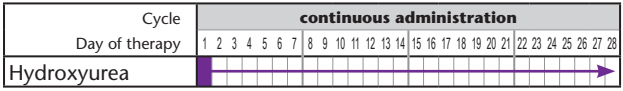
Chapter 6

Chronic Myelogenous Leukaemia

6 Chronic Myelogenous Leukaemia

6.1 HYDROXYUREA *XA149*

D	Drug	Do mg/kg	Di	V ml	T	R
1-*	Hydroxyurea	40	–	–	–	p.o.



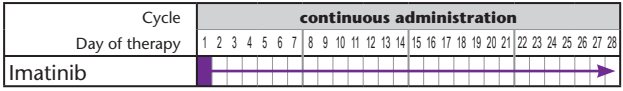
Repetition: * Continuous administration

Note:
- Dose adjustment according to response

Literature:
Hehlmann R. et al., Blood 84: 4064ff, 1994

6.2 IMATINIB (Chronic phase) *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Imatinib	400	–	–	–	p.o.



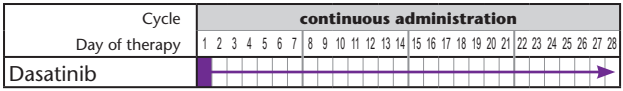
Repetition: * Continuous administration

Note:
- In accelerated phase CML, the initial dose is 600 mg daily.

Literature:
Druker B., N Engl J Med 344: 1031ff, 2001
O´Brien S. et al., N Engl J Med 348: 994ff, 2003

6.3 DASATINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Dasatinib	100	–	–	–	p.o.



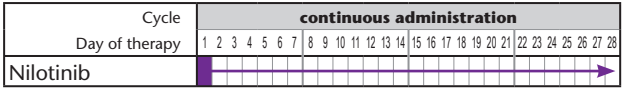
Repetition: * Continuous administration

Note:
- The total dose of 100 mg should be administered at once

Literature:
Shah N.P. et al., J Clin Oncol 26: 3204ff, 2008

6.4 NILOTINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Nilotinib	600	–	–	–	p.o.



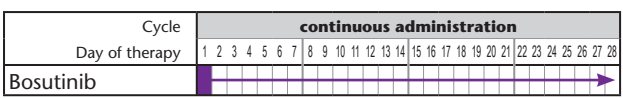
Repetition: * Continuous administration

Note:
- Nilotinib 600 mg divided into 2 equal doses, morning and evening

Literature:
Saglio G. et al., N Engl J Med 362: 2251ff, 2010

6.5 BOSUTINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Bosutinib	500	–	–	–	p.o.

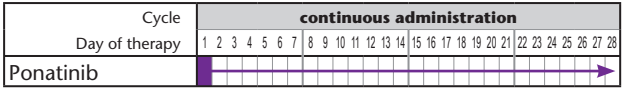


Repetition: * Continuous administration

Literature:
Cortes J.E. et al., J Clin Oncol 30: 3486ff, 2012

6.6 PONATINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Ponatinib	45	–	–	–	p.o.



Repetition: * Continuous administration

Literature:
Cortes J.E. et al., N Engl J Med 369: 1783ff, 2013

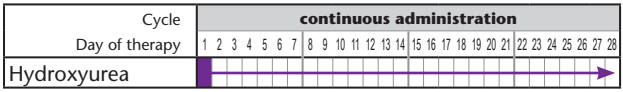
Chapter 7

Other Chronic Myeloproliferative Diseases

7 Other Chronic Myeloproliferative Diseases

7.1 HYDROXYUREA *XA149*

D	Drug	Do mg/kg	Di	V ml	T	R
1-*	Hydroxyurea	15	–	–	–	p.o.



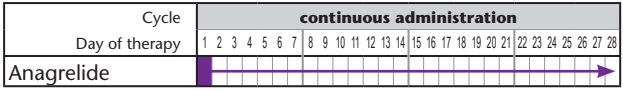
Repetition: * Continuous administration

Note:
- Dose adjustment according to response

Literature:
Cortelazzo S. et al., N Engl J Med 332: 1132ff, 1995

7.2 ANAGRELIDE *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Anagrelide	4 x 0.5	–	–	–	p.o.



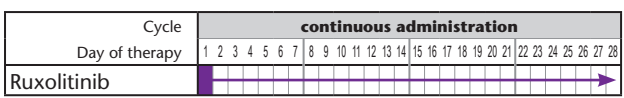
Repetition: * Continuous administration

Note:
- Start therapy with 0.5 mg/d for a week, thereafter increase the dose weekly by 0.5 mg/d until the desired therapeutic effect is achieved. The total dose per day to be administered should be divided into 2x (every 12 h) or 3x (every 8 h). The drug at a dose higher than 5 mg/d should not be given.

Literature:
Petitt R.M. et al., Semin Hematol 34: 51ff, 1997

7.3 RUXOLITINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Ruxolitinib	2 x 15#	–	–	–	p.o.



Repetition: * Continuous administration

Note:

- (#) The starting dose of Ruxolitinib is 15 mg given orally twice daily for patients with a platelet count between 100-200 G/L and 20 mg twice daily for patients with a platelet count > 200 G/L. Patients with a platelet count between 50-100 G/L should be started with 5 mg twice daily.

Literature:

Verstovsek S. et al., N Engl J Med 366: 799ff, 2012

B Oncology

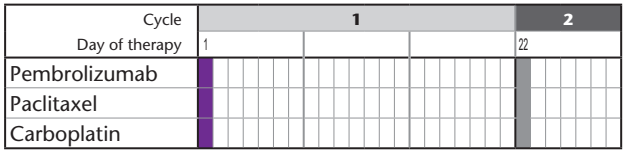
Chapter 1

Lung Cancer

1.1 Non-small Cell Lung Cancer – NSCLC

1.1.1 PEMBROLIZUMAB + CARBOPLATIN / PACLITAXEL *XA081 + XC204*

D	Drug	Do	Di	V ml	T	R
1	Pembrolizumab	200 mg	0.9% NaCl	100	30'	i.v.
1	Paclitaxel	200 mg/m²	0.9% NaCl	500	3h	i.v.
1	Carboplatin	AUC 6	5% Glucose	500	1h	i.v.



Repetition: Day 22

Number of cycles: Carboplatin/Paclitaxel: 4;
Pembrolizumab: up to 35

Note:
- Pembrolizumab should be dissolved at 1 - 10 mg/ml
- Paclitaxel accompanying medication:
- *Premedication:* Dexamethasone 20 mg i.v. 30 min before Paclitaxel, or Dexamethasone 20 mg orally 12h and 6h before Paclitaxel. Additional premedication with 40 mg Famotidine and 30 mg Diphenhydramine is recommended.
- Diluted Paclitaxel solutions should be administered through non PVC-containing administration sets.

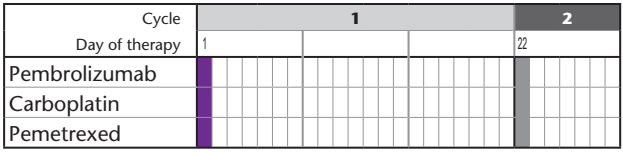
- Calculation of Carboplatin dose (Calvert):
  Dose (mg) = target AUC x (GFR + 25)

Literature:

Paz-Ares L. et al., N Engl J Med 379: 2040ff, 2018

1.1.2 PEMBROLIZUMAB + CARBOPLATIN / PEMETREXED *XA081 + XC206*

D	Drug	Do	Di	V ml	T	R
1	Pembrolizumab	200 mg	0.9% NaCl	100	30'	i.v.
1	Carboplatin	AUC 6	5% Glucose	500	1h	i.v.
1	Pemetrexed	500 mg/m²	0.9% NaCl	100	10'	i.v.



Repetition: Day 22

Number of cycles: Carboplatin: 4;
Pembrolizumab/Pemetrexed: up to 35

Note:
- Pembrolizumab should be dissolved at 1 - 10 mg/ml
- 1-3 weeks prior to start of therapy with Premetrexed substitution with 350 µg - 1000 µg folic acid orally daily till 3 weeks after completion of therapy
  Substitution with vitamin B12: 1000 µg i.m. (1 week preceding the first dose of pemetrexed and once every 9 weeks thereafter) till 3 weeks after completion of therapy
  Oral administration of dexamethasone 8 mg p.o. daily for 3 days starting on day 1 before Pemetrexed administration.

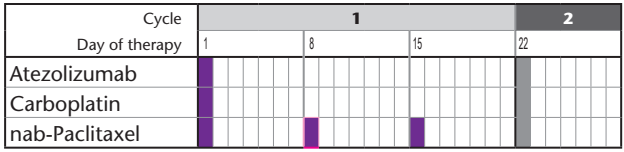
- Calculation of Carboplatin dose (Calvert):
  Dose (mg) = target AUC x (GFR + 25)

Literature:

Borghaei H. et al., J Thorac Oncol 14: 124ff, 2019

1.1.3 ATEZOLIZUMAB/CARBOPLATIN/ nab-PACLITAXEL *XA054 + XC205*

D	Drug	Do	Di	V ml	T	R
1	Atezolizumab	1200 mg	0.9% NaCl	250	30'*	i.v.
1	Carboplatin	AUC 6	5% Glucose	500	1h	i.v.
1,8, 15	nab-Paclitaxel	100 mg/m²	–	–	30'	i.v.



Repetition: Day 22

Number of cycles: 4-6, Atezolizumab until progressive disease or intolerability

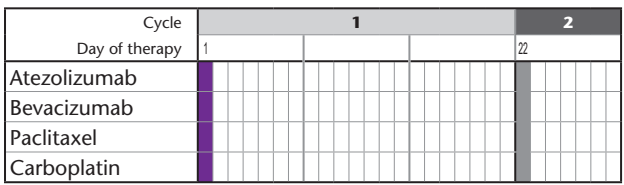
Note:
- (*) Atezolizumab: The initial dose should be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min. Atezolizumab should be dissolved at 4.4 mg/ml
- Calculation of Carboplatin dose (Calvert): Dose (mg) = target AUC x (GFR + 25)

Literature:
West H. et al., Lancet Oncol 20: 924ff, 2019

1.1.4 ATEZOLIZUMAB + BEVACIZUMAB + CARBOPLATIN / PACLITAXEL

XA054 + XA060 + XC204

D	Drug	Do	Di	V ml	T	R
1	Atezolizumab	1200 mg	0.9% NaCl	250	30'§	i.v.
1		15 mg/kg	0.9% NaCl	100	90'*	i.v.
1	Bevacizumab Paclitaxel	200# mg/m²	0.9% NaCl	500	3h	i.v.
1	Carboplatin	AUC 6	5% Glucose	500	1h	i.v.



Repetition: Day 22

Number of cycles: 4-6; Atezolizumab or Bevacizumab, or both until progressive disease or intolerability

Note:

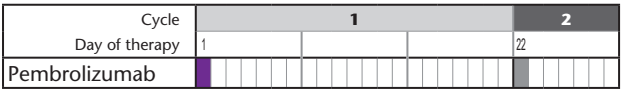
- (§) Atezolizumab: The initial dose should be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min. Atezolizumab should be dissolved at 4.4 mg/ml
- (*) Bevacizumab: The initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.
- Pembrolizumab should be dissolved at 1 - 10 mg/ml
- (#) Paclitaxel at a dose of 175 mg/m^2 for Asian patients
  Paclitaxel accompanying medication:
  Premedication: Dexamethasone 20 mg i.v. 30 min before Paclitaxel, or Dexamethasone 20 mg orally 12h and 6h before Paclitaxel. Additional premedication with 20 mg Famotidine and 30 mg Diphenhydramine is recommended.
- Diluted Paclitaxel solutions should be administered through non PVC-containing administration sets.
- Calculation of Carboplatin dose (Calvert):
  Dose (mg) = target AUC x (GFR + 25)

Literature:

Socinski M.A. et al., N Engl J Med 378: 2288ff, 2018

1.1.5 PEMBROLIZUMAB *XA081*

D	Drug	Do mg	Di	V ml	T	R
1	Pembrolizumab	200	0.9% NaCl	100	30'	i.v.



Repetition: Day 22

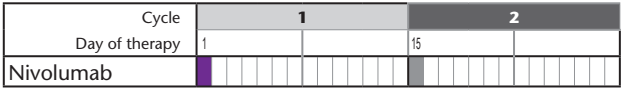
Number of cycles: Until progressive disease or intolerability

Note:
- Pembrolizumab should be dissolved at 1-10 mg/ml

Literature:
Reck M. et al., N Engl J Med 375: 1823ff, 2016

1.1.6 NIVOLUMAB *XA085*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Nivolumab*	3	0.9 NaCl	100	1h	i.v.



Repetition: Day 15

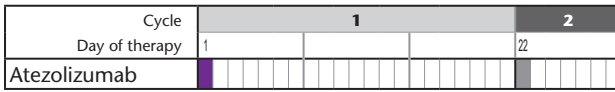
Number of cycles: Until progressive disease or intolerability

Note:
- Nivolumab should be dissolved at 1 - 10 mg/ml
- (*) Nivolumab can also be administered at 240 mg flat-dose every 2 weeks (Zhao X. et al., Ann Oncol 28: 2002ff, 2017) or at 480 mg every 4 weeks (Long G.V. et al.; Ann Oncol 29: 2208ff, 2018)

Literature:
Brahmer J. et al., N Engl J Med 373: 123ff, 2015

1.1.7 ATEZOLIZUMAB *XA054*

D	Drug	Do mg	Di	V ml	T	R
1	Atezolizumab	1200	0.9% NaCl	500	30'*	i.v.



Repetition: Day 22

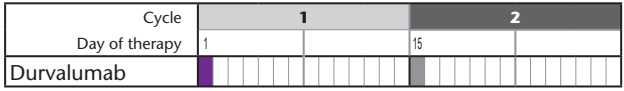
Number of cycles: Until progressive disease or intolerability

Note:
- (*) Atezolizumab: The initial dose should be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.
- Atezolizumab should be dissolved at 4.4mg/ml

Literature:
Rittmeyer A. et al., Lancet 389: 255ff, 2017

1.1.8 DURVALUMAB *XA117*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Durvalumab	10	0.9% NaCl	250	1h	i.v.



Repetition: Day 15

Number of cycles: For a maximum of 12 months

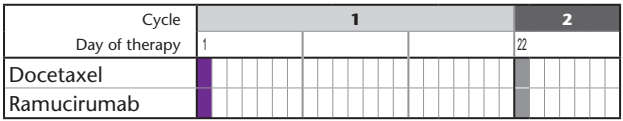
Note:
- Durvalumab at a concentration of 1 – 15 mg/ml

Literature:
Antonia S.J. et al., N Engl J Med 377: 1919ff, 2017

1.1.9 DOCETAXEL + RAMUCIRUMAB

XC412+ XA088

D	Drug	Do	Di	V ml	T	R
1	Docetaxel	75 mg/m²	0.9% NaCl	250	1h	i.v.
1	Ramucirumab	10 mg/kg	0.9% NaCl	500	1h	i.v.



Repetition: Day 22

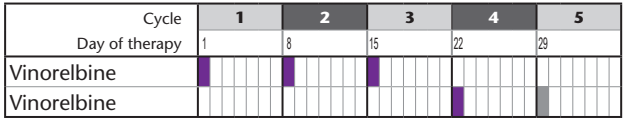
Number of cycles: 6

Note:
- Docetaxel should be dissolved at 0.3-0.74 mg/ml
- Accompanying medication: Dexamethasone 8 mg orally 2x daily for 3 days starting on day 1 before Docetaxel administration.

Literature:
Garon E.B. et al., Lancet 384: 665ff, 2014

1.1.10 VINORELBINE (oral) *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1,8, 15	Vinorelbine	60	–	–	–	p.o.
22-*	Vinorelbine	80	–	–	–	p.o.



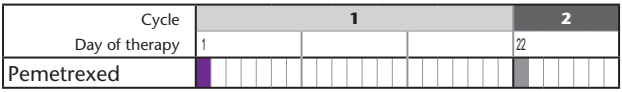
Repetition: * Weekly

Note:
- In case of neutropenia (once WHO grade 4 or twice consecutively WHO grade 3):
  - Within the first 3 weeks following treatment initiation: maintain dosage at 60 mg/m²/week
  - In case of subsequent weeks: reduce dose from 80 mg/m²/week to 60 mg/m²/week

Literature:
Jassem J. et al., Ann Oncol 12: 1375ff, 2001

1.1.11 PEMETREXED *XC800*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Pemetrexed	500	0.9% NaCl	100	10'	i.v.



Repetition: Day 22

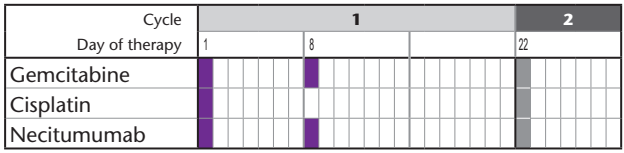
Number of cycles: 6

Note:
- 1-3 weeks prior to start of therapy with Pemetrexed
- Substitution with 350 µg - 1000 µg Folic Acid orally daily till 3 weeks after completion of therapy.
- Substitution with Vitamin B12: 1000 µg i.m. (once every 9 weeks) till 3 weeks after completion of therapy.
- Oral administration of Dexamethasone 8 mg p.o. daily for 3 days starting on day 1 before administration of Pemetrexed.

Literature:
Hanna N. et al., J Clin Oncol 22: 1589ff, 2004

1.1.12 GEMCITABINE / CISPLATIN + NECITUMUMAB *XC592 + XA115*

D	Drug	Do	Di	V ml	T	R
1,8	Gemcitabine	1250 mg/m²	0.9% NaCl	500	30'	i.v.
1	Cisplatin	75 mg/m²	0.9% NaCl	1000	2h	i.v.
1,8	Necitumumab	800 mg	0.9% NaCl	250	1h	i.v.



Repetition: Day 22

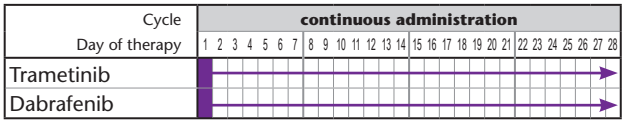
Number of cycles: 6

Note:
- Premedication: 30 mg Diphenhydramine i.v., 12 mg Dexamethasone i.v.; 1000 mg Paracetamol p.o.
- Cisplatin (only if GFR ≥60 ml/ min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature:
Thatcher N. et al., Lancet Oncol. 16: 763ff, 2015

1.1.13 TRAMETINIB / DABRAFENIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Trametinib	2	–	–	–	p.o.
1-*	Dabrafenib	300#	–	–	–	p.o.



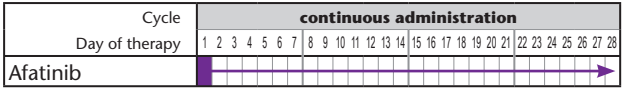
Repetition: * Continuous administration

Note:
- (#) Divided into 2 equal doses

Literature:
Planchard D. et al., Lancet Oncol 18: 1307ff, 2017

1.1.14 AFATINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Afatinib	40	–	–	–	p.o.



Repetition: * Continuous administration

Literature:
Sequist L.V. et al., J Clin Oncol 31: 3327ff, 2013

1.1.15 OSIMERTINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Osimertinib	80	–	–	–	p.o.

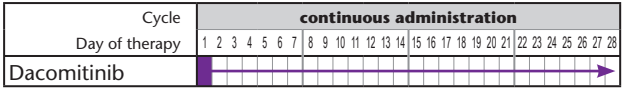
Cycle	continuous administration
Day of therapy	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
Osimertinib	

Repetition: * Continuous administration

Literature:
Mok Y.L. et al., N Engl J Med 376: 629ff, 2017

1.1.16 DACOMITINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Dacomitinib	45	–	–	–	p.o.

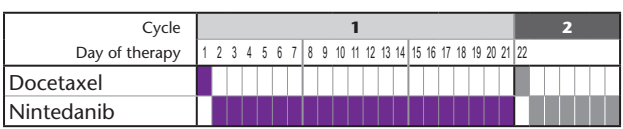


Repetition: * Continuous administration

Literature:
Wu Y.L. et al.; Lancet Oncol 18: 1454ff, 2017

1.1.17 NINTEDANIB / DOCETAXEL *XC412*

D	Drug	Do	Di	V ml	T	R
1	Docetaxel	75 mg/m²	0.9 NaCl	250	1h	i.v.
2-21	Nintedanib	400 mg	–	–	–	p.o.



Repetition: Day 22

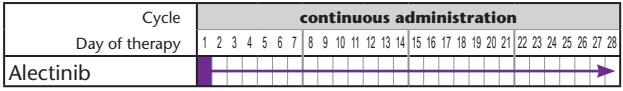
Number of cycles: 6

Note:
- Docetaxel should be dissolved at 0.3 - 0.74 mg/ml
- *Accompanying medication:* Dexamethasone 8 mg orally 2x daily for 3 days starting on day 1 before Docetaxel administration.
- Nintedanib is administered at 200 mg twice daily. Patients who discontinue combination therapy because of docetaxel-related adverse events may continue Nintedanib monotherapy if at least 4 cycles of combination therapy were administered.

Literature:
Reck M. et al., Lancet Oncol 15: 143ff; 2014

1.1.18 ALECTINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Alectinib	1200#	–	–	–	p.o.



Repetition: * Continuous administration

Note:

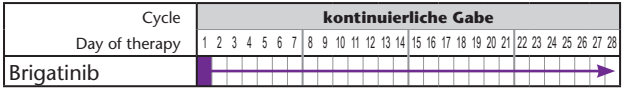
- (#) 600 mg (four 150 mg capsules) taken twice daily with food

Literature:

Peters S. et al., N Engl J Med 377: 829ff, 2017
Camidge D.R. et al., J Thorac Oncol 14: 1233ff, 2019

1.1.19 BRIGATINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Brigatinib	180#	–	–	–	p.o.



Repetition: * Continuous administration

Note:

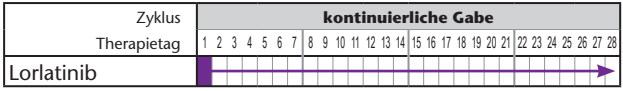
- (#) The recommended starting dose of Brigatinib is 90 mg once daily for the first 7 days, then 180 mg once daily

Literature:

Camidge D.R. et al., N Engl J Med 379: 2017ff, 2018

1.1.20 LORLATINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Lorlatinib	100	–	–	–	p.o.



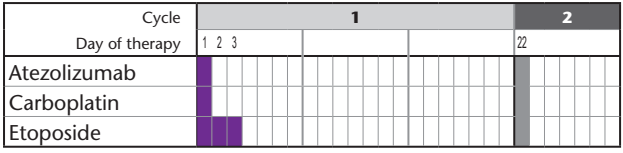
Repetition: * Continuous administration

Literature:
Solomon B.J. et al., Lancet Oncol 19: 1654ff, 2018

1.2 Small Cell Lung Cancer – SCLC

1.2.1 ATEZOLIZUMAB + CARBOPLATIN / ETOPOSIDE *XA054 + XC192*

D	Drug	Do	Di	V ml	T	R
1	Atezolizumab	1200 mg	0.9% NaCl	250	30'*	i.v.
1	Carboplatin	AUC 5	5% Glucose	500	1h	i.v.
1-3	Etoposide	100 mg/m²	0.9% NaCl	500	1h	i.v.



Repetition: Day 22

Number of cycles: 4-6; Atezolizumab until progressive disease or intolerability

Note:

- (*) Atezolizumab: The initial dose should be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min. Atezolizumab should be dissolved at 4.4 mg/ml
- Calculation of Carboplatin dose (Calvert): Dose (mg) = target AUC x (GFR + 25)
- Etoposide should be dissolved in 1000 ml 0.9% NaCl if total dose is ≥ 200 mg.

Literature: Horn L. et al., N Engl J Med 379: 2220ff, 2018

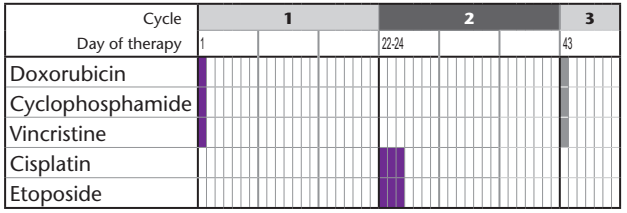
1.2.2 EVANS

CAV *XC032*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Doxorubicin	50	0.9% NaCl	500	1h	i.v.
1	Cyclophosphamide	1000	0.9% NaCl	1000	2h	i.v.
1	Vincristine	1.4*	0.9% NaCl	100	10'	i.v.

CISPLATIN / ETOPOSIDE *XC304*

D	Drug	Do mg/m²	Di	V ml	T	R
1-3	Cisplatin	25	0.9% NaCl	500	1h	i.v.
1-3	Etoposide	100	0.9% NaCl	500	1h	i.v.



Repetition: Day 22 (alternating)

Number of cycles: 6 (3x CAV
and 3x Cisplatin/ Etoposide alternatingly)

Note:

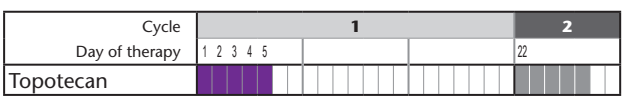
- Cisplatin (only if GFR ≥60 ml/ min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative dose ≥500 mg/m^2
- (*) Vincristine max. 2 mg total doses
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide
- Etoposide should be dissolved in 1000 ml 0.9% NaCl if total dose is ≥ 200 mg

Literature:

Evans W.K. et al., Ann Int Med 107: 451ff, 1987

1.2.3 TOPOTECAN *XC840*

D	Drug	Do mg/m²	Di	V ml	T	R
1-5	Topotecan	1.5	0.9% NaCl	100	30'	i.v.



Repetition: Day 22

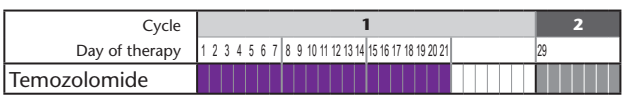
Number of cycles: 6

Note:
- Topotecan should be dissolved at 0.025 - 0.05 mg/ml

Literature:
Ardizzoni A. et al., J Clin Oncol 15: 2090ff, 1997

1.2.4 TEMOZOLOMIDE *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1-21	Temozolomide	75	–	–	–	p.o.



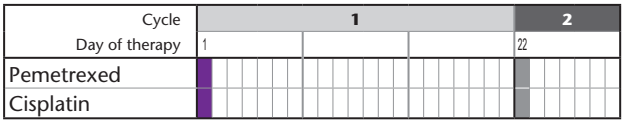
Repetition: Day 29

Literature:
Pietanza C. et al., Clin Cancer Res 18: 1138ff, 2012

1.3 MESOTHELIOMA

1.3.1 PEMETREXED / CISPLATIN *XC326*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Pemetrexed	500	0.9% NaCl	100	10'	i.v.
1	Cisplatin	75	0.9% NaCl	500	1h	i.v.



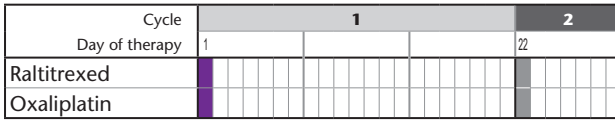
Repetition: Day 22
Number of cycles: 6
Note:

- 1-3 weeks prior to start of therapy with Pemetrexed
- Substitution with 350 µg - 1000 µg Folic Acid orally daily till 3 weeks after completion of therapy.
- Substitution with Vitamin B12: 1000 µg i.m. (once every 9 weeks) till 3 weeks after completion of therapy.
- Oral administration of Dexamethasone 8 mg p.o. daily for 3 days starting on day 1 before administration of Pemetrexed.
- Cisplatin (only if GFR ≥60 ml/min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature: Vogelzang N.J. et al., J Clin Oncol 21:2636ff, 2003

1.3.2 OXALIPLATIN / RALTITREXED *XC760*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Raltitrexed	3	0.9% NaCl	100	15'	i.v.
1	Oxaliplatin	130	5% Glucose	500	2h	i.v.



Repetition: Day 22

Number of cycles: 4-6

Note:
- *Caution:* Oxaliplatin should be administered 1 hour after Raltitrexed.

Literature:
Fizazi K. et al., J Clin Oncol 18: 2293ff, 2000

1.3.3 CISPLATIN / RALTITREXED *XC812*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Raltitrexed	3	0.9% NaCl	100	15'	i.v.
1	Cisplatin	80	0.9% NaCl	500	1h	i.v.

Cycle	1	2
Day of therapy	1	22
Raltitrexed		
Cisplatin		

Repetition: Day 22

Number of cycles: 6

Note:
- Cisplatin (only if GFR ≥60 ml/min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature:
Van Meerbeeck J.P. et al., J Clin Oncol 23: 6881ff, 2005

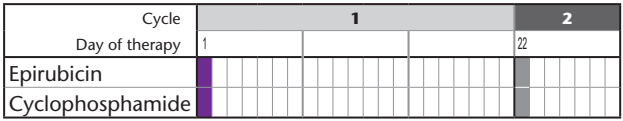
Chapter 2

Breast Cancer

2.1 EC / DOCETAXEL

XC364 (EC) + XC416 (Docetaxel)

D	Drug	Do mg/m²	Di	V ml	T	R
1	Epirubicin	90	0.9% NaCl	250	30'	i.v.
1	Cyclophosphamide	600	0.9% NaCl	500	1h	i.v.



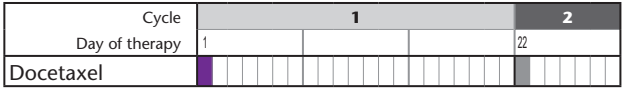
Repetition: Day 22

Number of cycles: 4

Note:

- *Caution:* Cardiac toxicity of Epirubicin at cumulative dose ≥1000 mg/m²
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide

D	Drug	Do mg/m²	Di	V ml	T	R
1	Docetaxel	100	0.9% NaCl	250	1h	i.v.



Repetition: Day 22

Number of cycles: 4

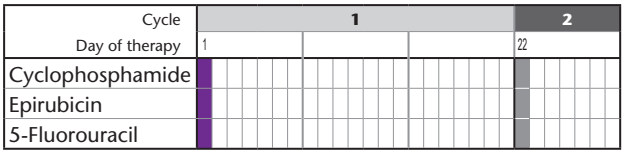
Note:
- Docetaxel should be dissolved at 0.3-0.74 mg/ml
- *Accompanying medication:* Dexamethasone 8 mg orally 2x daily for 3 days starting on day 1 before Docetaxel administration.

Literature:
Nitz U. et al., Ann Oncol 25: 1551ff, 2014

2.2 FEC / PERTUZUMAB / TRASTUZUMAB / DOCETAXEL (TRYPHAENA)

XC532 (FEC); XA082 + XA100 + XC412 (Pertuzumab/Trastuzumab/Docetaxel)

D	Drug	Do mg/m²	Di	V ml	T	R
1	Cyclophosphamide	600	0.9 NaCl	500	1h	i.v.
1	Epirubicin	100	0.9 NaCl	250	30'	i.v.
1	5-Fluorouracil	500	0.9 NaCl	100	20'	i.v.



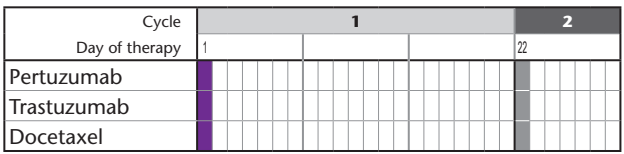
Repetition: Day 22

Number of cycles: 3

Note:

- *Caution:* Cardiac toxicity of Epirubicin at cumulative dose ≥ 1000 mg/m²
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide

D	Drug	Do	Di	V ml	T	R
1	Pertuzumab	420 mg*	0.9 NaCl	250	1h	i.v.
1	Trastuzumab	6 mg/kg#	0.9 NaCl	500	90'	i.v.
1	Docetaxel	75 mg/m²	0.9 NaCl	250	1h	i.v.



Repetition: Day 22

Number of cycles: 3

Note:

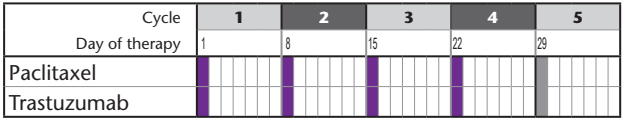
- (*) Pertuzumab „fixed loading dose" of 840 mg at initial administration over 60 min. If well tolerated, subsequent doses can be administered over 30 min.
- (#) Trastuzumab „loading dose" of 8 mg/kg at initial administration over 90 min. If well tolerated, subsequent doses can be administered over 30 min.
- Trastuzumab can also be administered subcutaneously at a fixed dose of 600 mg/5 ml.
- Docetaxel should be dissolved at 0.3-0.74 mg/ml
- *Accompanying medication:* Dexamethasone 8 mg orally 2x daily for 3 days starting on day 1 before Docetaxel administration.
- *Optional:* Carboplatin/Docetaxel + Pertuzumab/ Trastuzumab x 6

Literature: Schneeweiß A. et al., Ann Oncol 24: 2278ff, 2013

2.3 PACLITAXEL + TRASTUZUMAB

XC768 + XA100

D	Drug	Do	Di	V ml	T	R
1	Paclitaxel	80 mg/m²	0.9% NaCl	250	3h	i.v.
1	Trastuzumab	2 mg/kg*	0.9% NaCl	250	90'	i.v.



Repetition: Day 8

Number of cycles: 12

Note:

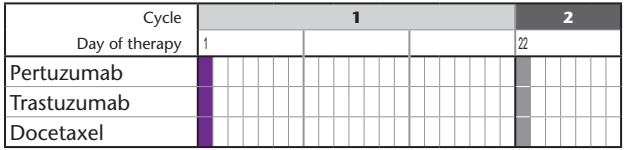
- (*) Trastuzumab „loading dose" of 4 mg/kg at initial administration over 90 min. If well tolerated, subsequent doses can be administered over 30 min.
- After the completion of 12 weeks of induction treatment, Trastuzumab can be changed to 6 mg/kg every 3 weeks for 40 weeks.
- Trastuzumab can also be administered subcutaneously at a fixed dose of 600 mg/5 ml.

Literature:

Tolaney S.M. et al., N Engl J Med 372: 134ff, 2015
Ismael G. et al., Lancet Oncol 13: 869ff, 2012

2.4 PERTUZUMAB / TRASTUZUMAB / DOCETAXEL *XA082 + XA100 + XC412*

D	Drug	Do	Di	V ml	T	R
1	Pertuzumab	420 mg*	0.9% NaCl	250	1h	i.v.
1	Trastuzumab	6 mg/kg#	0.9% NaCl	500	90'	i.v.
1	Docetaxel	75 mg/m²	0.9% NaCl	250	1h	i.v.



Repetition: Day 22

Number of cycles: 6

Note:
- (*) Pertuzumab „fixed loading dose" of 840 mg at initial administration over 60 min. If well tolerated, subsequent doses can be administered over 30 min.
- (#) Trastuzumab „loading dose" 8mg/kg at initial administration over 90 min. If well tolerated, subsequent doses can be administered over 30 min.
- Trastuzumab can also be administered subcutaneously at a fixed dose of 600 mg/5 ml
- Docetaxel should be dissolved at 0.3 – 0.74 mg/ml

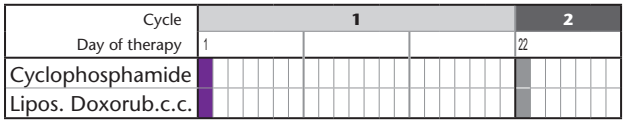
- *Accompanying medication:*
  Dexamethasone 8 mg orally 2x daily for 3 days starting on day 1 before Docetaxel administration

Literature:

Baselga J. et al., N Engl J Med 366: 109ff, 2012
Swain S.M. et al., Lancet Oncol 14: 461ff, 2013
Ismael G. et al., Lancet Oncol 13: 869ff, 2012

2.5 CYCLOPHOSPHAMIDE / LIPOSOMAL DOXORUBICIN CITRATE COMPLEX *XC452*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Cyclophosphamide	600	0.9% NaCl	500	1h	i.v.
1	Liposomal Doxorubicin citrate complex (Myocet®)	60	0.9% NaCl	100	1h	i.v.



Repetition: Day 22

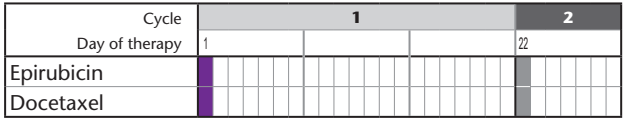
Number of cycles: *6*

Note:
- Liposomal Doxorubicin citrate complex should be dissolved at 0.4 - 1.2 mg/ml
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide

Literature:
Batist G. et al., J Clin Oncol 19: 1444ff, 2001

2.6 EPIRUBICIN / DOCETAXEL *XC424*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Epirubicin	75	0.9% NaCl	500	1h	i.v.
1	Docetaxel	75	0.9% NaCl	250	1h	i.v.



Repetition: Day 22

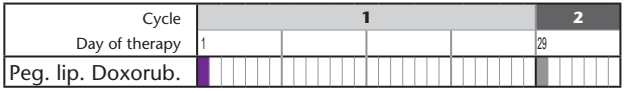
Number of cycles: 6

Note:
- Docetaxel should be dissolved at 0.3 - 0.74 mg/ml
- *Caution:* Cardiac toxicity of Epirubicin at cumulative dose ≥1000 mg/m²
- *Accompanying medication:*
  Dexamethasone 8 mg orally 2x daily for 3 days starting on Day 1 before Docetaxel administration

Literature:
Bonneterre J., Br J Cancer 91: 1466ff, 2004

2.7 PEGYLATED LIPOSOMAL DOXORUBICIN *XC452*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Pegylated liposomal Doxorubicin (Caelyx®)	50	5% Glucose	500	1h	i.v.



Repetition: Day 29

Number of cycles: 6

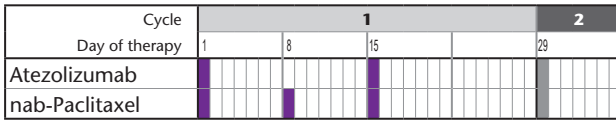
Note:
- Pegylated liposomal Doxorubicin should be dissolved in 250 ml of 5% Glucose if total dose is ≤90 mg and in 500 ml of 5% Glucose in case the total dose exceeds 90 mg.

Literature:
O´Brien M.E., Ann Oncol 15: 440ff, 2004

2.8 ATEZOLIZUMAB + nab-PACLITAXEL

XA054 + XC774

D	Drug	Do	Di	V ml	T	R
1,15	Atezolizumab	840 mg	0.9% NaCl	250	30'*	i.v.
1,8, 15	nab-Paclitaxel	100 mg/m²	–	–	30'	i.v.



Repetition: Day 29

Number of cycles: Nab-Paclitaxel: 6;
Atezolizumab: Until progressive disease or intolerability

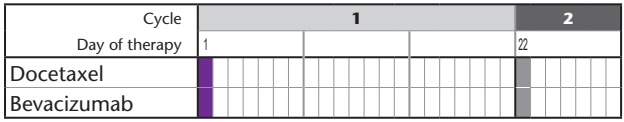
Note:
- (*) Atezolizumab: The initial dose should be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.
- Atezolizumab should be dissolved at 4.4 mg/ml

Literature:
Schmid P. et al., N Engl J Med 379: 2108ff, 2018

2.9 DOCETAXEL / BEVACIZUMAB

XC416 + XA060

D	Drug	Do	Di	V ml	T	R
1	Docetaxel	100 mg/m²	0.9% NaCl	250	1h	i.v.
1	Bevacizumab	15 mg/kg	0.9% NaCl	100	90'*	i.v.



Repetition: Day 22

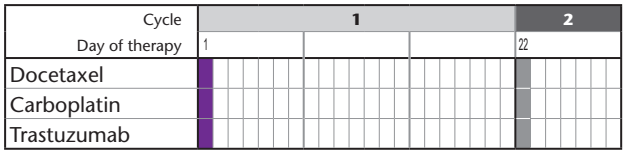
Number of cycles: 6,
optional: Bevacizumab until progressive disease or intolerability

Note:
- Docetaxel should be dissolved at 0.3 - 0.74 mg/ml
- *Accompanying medication:*
  Dexamethasone 8 mg orally 2x daily for 3 days starting one day before Docetaxel administration.
- (*) Bevacizumab: The initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min.
  If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.

Literature:
Miles D., J Clin Oncol 28: 3239ff, 2010

2.10 DOCETAXEL / CARBOPLATIN / TRASTUZUMAB *XA100 + XC184*

D	Drug	Do	Di	V ml	T	R
1	Docetaxel	75 mg/m²	0.9% NaCl	250	1h	i.v.
1	Carboplatin	AUC 6	5% Glucose	500	30'	i.v.
1	Trastuzumab	6 mg/kg*	0.9% NaCl	250	90'	i.v.



Repetition: Day 22

Number of cycles: Trastuzumab adjuvant over 1 year; Docetaxel and Carboplatin for 6 cycles

Note:
- Docetaxel should be dissolved at 0.3 – 0.74 mg/ml
- *Accompanying medication:*
  Dexamethasone 8 mg orally 2x daily for 3 days starting one day before Docetaxel administration.
- Calculation of Carboplatin dose (Calvert):
  Dose (mg) = target AUC x (GFR + 25)

- (*) Trastuzumab „loading dose“ 8 mg/kg at initial administration over 90 min. If well tolerated, subsequent doses can be administered over 30 min.
- Trastuzumab can also be administered subcutaneously at a fixed dose of 600 mg/5 ml.

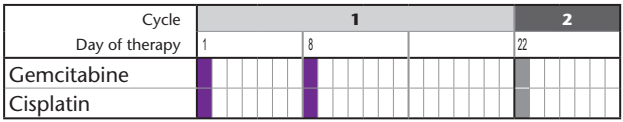
Literature:

Slamon D. et al., N Engl J Med. 365: 1273ff, 2011
Ismael G. et al., Lancet Oncol 13: 869ff, 2012

2.11 GEMCITABINE / CISPLATIN

XC592 (Day 1), XC592 (Day 8)

D	Drug	Do mg/m²	Di	V ml	T	R
1,8	Gemcitabine	750	0.9% NaCl	500	30'	i.v.
1,8	Cisplatin	30	0.9% NaCl	500	1h	i.v.



Repetition: Day 22

Number of cycles: 6

Note:

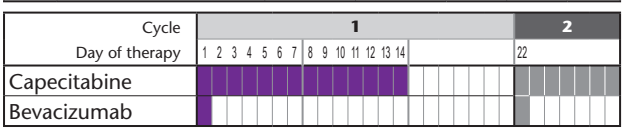
- Cisplatin (only if GFR ≥60 ml/min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature:

Nagourney RA et al., J Clin Oncol, 18: 2245ff, 2000

2.12 CAPECITABINE + BEVACIZUMAB *XA060*

D	Drug	Do	Di	V ml	T	R
1-14	Capecitabine	2000 mg/m²	–	–	–	p.o.
1	Bevacizumab	15 mg/kg	0.9% NaCl	100	90'*	i.v.



Repetition: Day 22

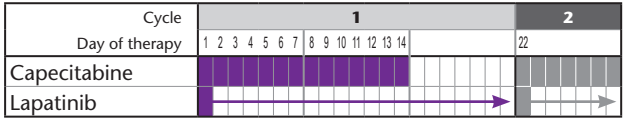
Number of cycles: 6

Note:
- Capecitabine: 2000 mg/m² divided into 2 equal doses, morning and evening within 30 min after a meal
- (*) Bevacizumab: The initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.

Literature:
Robert J.N. et al., J Clin Oncol 29: 1252ff, 2011

2.13 CAPECITABINE / LAPATINIB *XA149*

D	Drug	Do	Di	V ml	T	R
1-14	Capecitabine	2000 mg/m²	–	–	–	p.o.
1-*	Lapatinib	1250 mg (absolute)	–	–	–	p.o.



Repetition: Capecitabine Day 22
* Lapatinib continuous administration

Number of cycles: 6

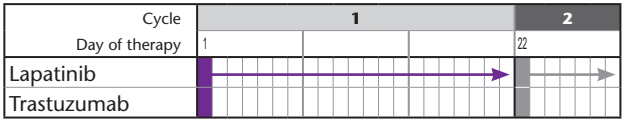
Note:
- Capecitabine: 2000 mg/m² divided into 2 equal doses, morning and evening within 30 min after a meal

Literature:
Geyer C.E. et al., N Engl J Med 355: 2733ff, 2006

2.14 LAPATINIB / TRASTUZUMAB

XA149 + XA100

D	Drug	Do	Di	V ml	T	R
1-*	Lapatinib	1000 mg (absolute)	–	–	–	p.o.
1	Trastuzumab	6 mg/kg#	0.9% NaC	250	90'	i.v.



Repetition: * Lapatinib continuous administration
Trastuzumab Day 22

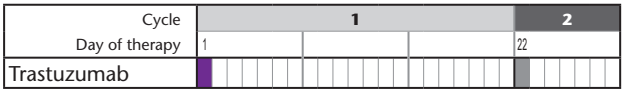
Number of cycles: 6

Note:
- (#) Trastuzumab „loading dose" 8 mg/kg at initial administration over 90 min. If well tolerated, subsequent doses can be administered over 30 min.
- Trastuzumab can also be administered subcutaneously at a fixed dose of 600 mg/5 ml.

Literature:
Blackwell K.L. et al., J Clin Oncol 28: 1124ff, 2010
Ismael G. et al., Lancet Oncol 13: 869ff, 2012

2.15 TRASTUZUMAB *XA100*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Trastuzumab	6*	0.9% NaCl	250	90'*	i.v.



Repetition: Day 22

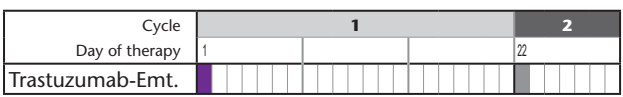
Number of cycles: Continuous administration over 12 months

Note:
- (*) Trastuzumab „loading dose“ 8 mg/kg at initial administration over 90 min. If well tolerated, subsequent doses can be administered over 30 min.
- Trastuzumab can also be administered subcutaneously at a fixed dose of 600 mg/5 ml.

Literature:
Piccart-Gebhard M.J. et al., N Engl J Med 353: 1659ff, 2005
Romond E.H. et al., N Engl J Med 353: 1673ff, 2005
Ismael G. et al., Lancet Oncol 13: 869ff, 2012

2.16 TRASTUZUMAB-EMTANSINE *XA112*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Trastuzumab-Emtansine	3.6	0.9% NaCl	250	90'*	i.v.



Repetition: Day 22

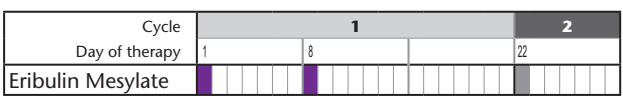
Number of cycles: Until progressive disease or intolerability

Note:
- (*) Initial administration of Trastuzumab-Emtasine over 90 min. If well tolerated, subsequent doses can be administered over 30 min.
- Use of in-line filter is required.

Literature:
Verma S. et al., N Engl J Med 367: 1783ff, 2012
von Minckwitz G. et al., N Engl J Med 379: 2108ff, 2019

2.17 ERIBULIN MESYLATE *XA494*

D	Drug	Do mg/m²	Di	V ml	T	R
1,8	Eribulin Mesylate*	1.4	0.9% NaCl	50	2-5'	i.v.



Repetition: Day 22

Number of cycles: 6

Note:
- (*) equivalent Eribulin dose of 1.23 mg/m² d1, 8

Literature:
Cortes J. et al., Lancet 377: 914ff, 2011

2.18 nab-PACLITAXEL *XC774*

D	Drug	Do mg/m²	Di	V ml	T	R
1	nab-Paclitaxel	260	–	–	30'	i.v.

Cycle	1	2
Day of therapy	1	22
nab-Paclitaxel		

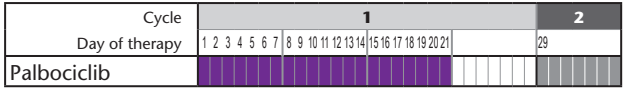
Repetition: Day 22

Number of cycles: 6

Literature:
Gradishar W.J. et al., J Clin Oncol 23: 7794, 2005

2.19 PALBOCICLIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-21	Palbociclib	125	–	–	–	p.o.



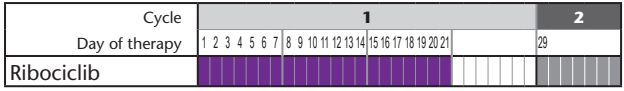
Repetition: Day 29

Note:
- Administration only in combination with an endocrine therapy

Literature:
Turner N.C. et al. N Engl J Med 373: 209ff, 2015

2.20 RIBOCICLIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-21	Ribociclib	600	–	–	–	p.o.



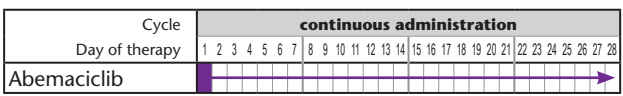
Repetition: Day 29

Note:
- The recommended dose is 600mg (three 200 mg film-coated tablets) of ribociclib once daily. Ribociclib should be used together with an aromatase inhibitor.

Literature:
Hortobagyi G.N. et al., N Engl J Med 375: 1738ff, 2016

2.21 ABEMACICLIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Abemaciclib	300	–	–	–	p.o.



Repetition: * Continuous administration

Note:
- The recommended dose of Abemaciclib is 150 mg twice daily.
  Administration only in combination with endocrine therapy.

Literature:
Goetz M.P. et al., J Clin Oncol 35: 3638ff, 2017
Sledge G.W. et al., J Clin Oncol 35: 2875ff, 2017

2.22 TALAZOPARIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Talazoparib	1	–	–	–	p.o.

Cycle	continuous administration
Day of therapy	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
Talazoparib	

Repetition: * kontinuierliche Gabe

Literature:
Litton J.K. et al., N Engl J Med 379: 753ff, 2018

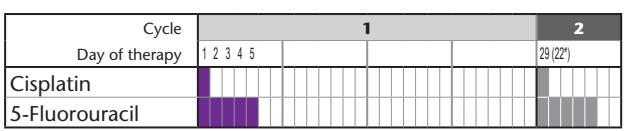
Chapter 3

Gastrointestinal Tumors

3.1 Esophageal Cancer

3.1.1 5FU / CISPLATIN *XC284*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Cisplatin	100	0.9% NaCl	500	2h	i.v.
1-5	5-Fluorouracil	1000	0.9% NaCl	1000	24h	i.v.



Repetition: Day 29 (22*)

Number of cycles: 6

Note:

- Cisplatin (if GFR ≥60 ml/ min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

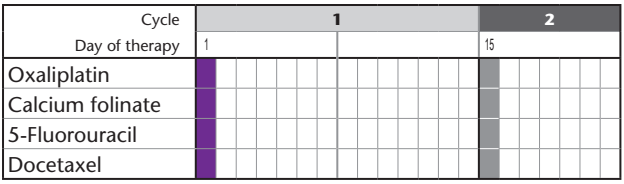
Literature:

(* Bleiberg H. et al., Eur J Cancer 33: 1216ff, 1997)
Kelsen D.P. et al., N Engl J Med 339: 1979ff, 1998

3.2 Gastric Cancer

3.2.1 5FU / LEUCOVORIN / OXALIPLATIN / DOCETAXEL (FLOT) *XC546*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Oxaliplatin	85	5% Glucose	500	2h	i.v.
1	Calcium folinate*	200	0.9 NaCl	250	2h	i.v.
1	5-Fluorouracil	2600	0.9 NaCl	500	24h	i.v.
1	Docetaxel	50	0.9 NaCl	250	1h	i.v.



Repetition: Day 15

Number of cycles: 8 [4 preoperatively and 4 postoperatively]

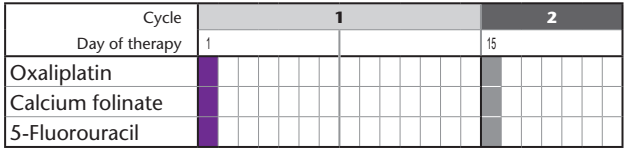
Note:

- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU
- Docetaxel should be dissolved at 0.3-0.74 mg/ml
- *Accompanying medication:* Dexamethasone 8 mg orally 2x daily for 3 days starting on day 1 before Docetaxel administration.

Literature: Al-Batran S.E. et al., Lancet 393: 1948ff, 2019

3.2.2 5FU / LEUCOVORIN / OXALIPLATIN (FLO)
XC752

D	Drug	Do mg/m²	Di	V ml	T	R
1	Oxaliplatin	85	5% Glucose	500	2h	i.v.
1	Calcium folinate*	200	0.9% NaCl	250	2h	i.v.
1	5-Fluorouracil	2600	0.9% NaCl	500	24h	i.v.



Repetition: Day 15

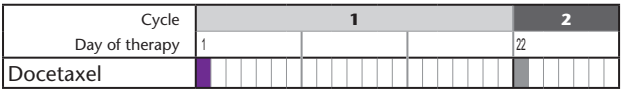
Number of cycles: 6

Note:
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU

Literature:
Al-Batran S.E. et al., J Clin Oncol 26:1435ff, 2008

3.2.3 DOCETAXEL *XC412*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Docetaxel	75	0.9 NaCl	250	1h	i.v.



Repetition: Day 22

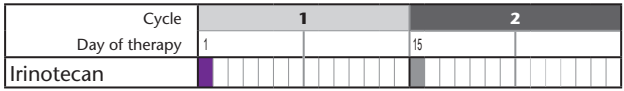
Number of cycles: 6

Note:
- Docetaxel should be dissolved at 0.3 - 0.74 mg/ml
- *Accompanying medication:* Dexamethasone 8 mg orally 2x daily for 3 days starting on day 1 before Docetaxel administration.

Literature:
Ford H.E.R. et al., Lancet Oncol 15: 78ff, 2014

3.2.4 IRINOTECAN *XC660*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Irinotecan	150	0.9% NaCl	500	90'	i.v.



Repetition: Day 15

Number of cycles: Until progressive disease or intolerability

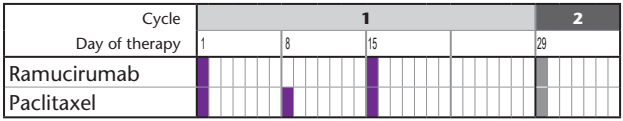
Note:
- *Caution:* Irinotecan can lead to life-threatening diarrhea and cholinergic symptoms. Diarrhea can appear either as acute reaction or also some days after Irinotecan administration.
- Accompanying medication: Atropine 0.2 mg s.c. or i.v.
- In case of diarrhea: Loperamide initially 4 mg, thereafter 2 mg every 2 hours. Loperamide should be continued for 12 hours following resolution of the diarrhea. If it persists longer than 48 hours, or if there is fever, administration of Ciprofloxacin and hospitalisation is recommended.

Literature:
Kang J.H. et al., J Clin Oncol 30: 1513ff, 2012

3.2.5 PACLITAXEL / RAMUCIRUMAB

XC768 + XA088

D	Drug	Do	Di	V ml	T	R
1,15	Ramucirumab	8 mg/kg	0.9 NaCl	500	1h	i.v.
1,8, 15	Paclitaxel	80 mg/m²	0.9 NaCl	250	1h	i.v.



Repetition: Day 29

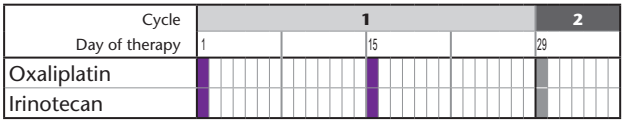
Note:
- Premedication with 30 mg Diphenhydramine recommended
- Ramucirumab can also be administered as monotherapy
- Paclitaxel should be dissolved at 0.3 - 1.2 mg/ml.
- *Paclitaxel-accompanying medication:*
  Dexamethasone 20 mg i.v. 30 min before Paclitaxel, or
  Dexamethasone 20 mg orally 6 h and 12 h before Paclitaxel.
  Additional premedication with 50 mg Ranitidine and 30 mg Diphenhydramine is recommended.
- Diluted Paclitaxel solutions should be administered through non PVC-containing administration sets.

Literature:

Wilke H.J. at al., Lancet Oncol 15: 1224ff, 2014
Fuchs C.S. et al., Lancet 383: 31ff, 2014

3.2.6 OXALIPLATIN / IRINOTECAN *XC672*

D	Drug	Do mg/m²	Di	V ml	T	R
1,15	Oxaliplatin	85	5% Glucose	500	2h	i.v.
1,15	Irinotecan	125	0.9% NaCl	500	30'	i.v.



Repetition: Day 29

Number of cycles: 6

Note:

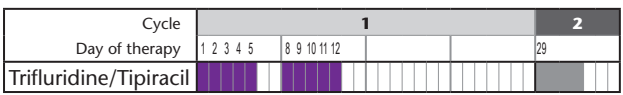
- *Caution:* Irinotecan can lead to life-threatening diarrhea and cholinergic symptoms. Diarrhea can appear either as acute reaction or also some days after Irinotecan administration.
- *Accompanying medication:* Atropine 0.2 mg s.c. or i.v.
- In case of diarrhea: Loperamide initially 4 mg, thereafter 2 mg every 2 hours. Loperamide should be continued for 12 hours following resolution of the diarrhea. If it persists longer than 48 hours, or if there is fever, administration of Ciprofloxacin and hospitalisation is recommended.

Literature:

Wöll E. et al., Anticancer Res 28: 2901ff, 2008

3.2.7 TRIFLURIDINE / TIPIRACIL *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1-5, 8-12	Trifluridine/Tipiracil	70	–	–	–	p.o.



Repetition: Day 29

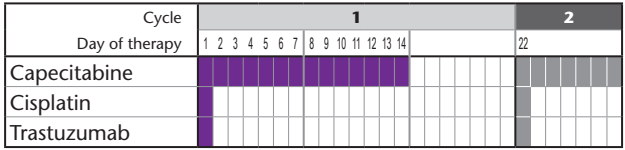
Number of cycles: Until progressive disease or intolerability

Note:
- Trifluridine/Tipiracil: 70 mg/m² divided into 2 equal doses, morning and evening.

Literature:
Shitara K. et al., Lancet Oncol 19: 1437ff, 2019

3.2.8 CAPECITABINE / 5FU + CISPLATIN + TRASTUZUMAB (ToGA) *XA280 + XA100*

D	Drug	Do	Di	V ml	T	R
1-14	Capecitabine	2000 mg/m²	–	–	–	p.o.
1	Cisplatin	80 mg/m²	0.9% NaCl	1000	2h	i.v.
1	Trastuzumab	6* mg/kg	0.9% NaCl	250	90'*	i.v.



Repetition: Day 22

Number of cycles: 6, Trastuzumab until progressive disease or intolerability

Note:

- Restricted to HER2 positive patients
- (*) Trastuzumab „loading dose" 8 mg/kg at initial administration over 90 min. If well tolerated, subsequent doses can be administered over 30 min.
- Trastuzumab can also be administered subcutaneously at a fixed dose of 600 mg/5 ml.
- Capecitabine: 2000 mg/m² divided into 2 equal doses, morning and evening within 30 min after a meal. As an alternative, Capecitabine can be substituted by 5FU: 5FU 800 mg/m²/d as continuous infusion on day 1-5 (repetition: q3w)

- Cisplatin (only if GFR ≥ 60 ml/min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

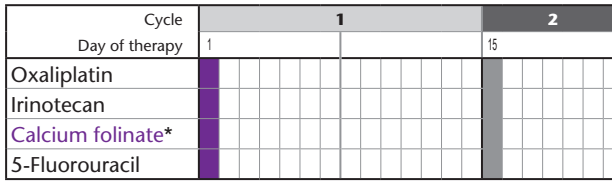
Literature:

Bang Y.J. et al., Lancet 376: 687ff, 2010
Ismael G. et al., Lancet Oncol 13: 869ff, 2012

3.3 Pancreatic Cancer and Cholangiocellular Carcinoma

3.3.1 Modified FOLFIRINOX *XC578*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Oxaliplatin	85	5% Glucose	500	2h	i.v.
1	Irinotecan	150	0.9% NaCl	500	90'	i.v.
1	Calcium folinate*	400	0.9% NaCl	250	2h	i.v.
1	5-Fluorouracil	2400	0.9% NaCl	500	46h	i.v.



Repetition: Day 15

Number of cycles: 12

Note:

- *Caution:* Irinotecan can lead to life-threatening diarrhea and cholinergic symptoms. Diarrhea can appear either as acute reaction or also some days after Irinotecan administration.
- *Accompanying medication:* Atropine 0.2 mg s.c. or i.v.

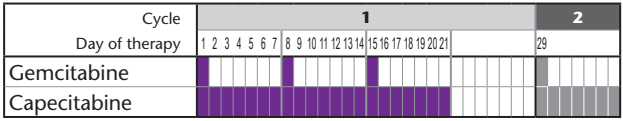
- In case of diarrhea: Loperamide initially 4 mg, thereafter 2 mg every 2 hours. Loperamide should be continued for 12 hours following resolution of the diarrhea. If it persists longer than 48 hours, or if there is fever, administration of Ciprofloxacin and hospitalisation is recommended.
- (*) Calcium folinate as modulator of 5FU should always be administered before 5FU.

Literature:

Conroy T. et al., N Engl J Med 379: 2395ff, 2018

3.3.2 GEMCITABINE / CAPECITABINE *XC592*

D	Drug	Do mg/m²	Di	V ml	T	R
1,8, 15	Gemcitabine	1000	0.9% NaCl	500	30'	i.v.
1-21	Capecitabine	1660	–	–	–	p.o.



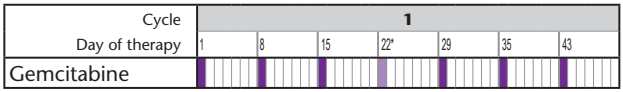
Repetition: Day 29

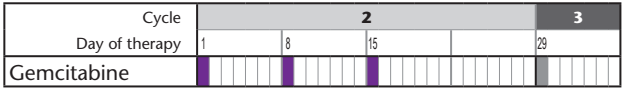
Note:
- Capecitabine: 1660 mg/m² divided into 2 equal doses, morning and evening within 30 min after a meal

Literature:
Neoptolemos J.P. et al., N Engl J Med 389: 1011ff, 2017

3.3.3 GEMCITABINE *XC592*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Gemcitabine	1000	0.9% NaCl	500	30'	i.v.





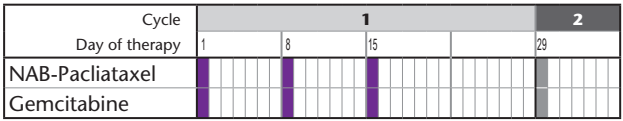
Repetition: weekly x 7 (the first cycle should be terminatd early if ≥ grade 2 non-hematologic or ≥ grade 3 hematologic toxicity); then day 1, 8, 15 repetition on day 29

Number of cycles: 6 (with cycle 1 over 7 weeks)

Literature:
Burris H.A. et al.; J Clin Oncol 15: 2403ff, 1997

3.3.4 nab-PACLITAXEL / GEMCITABINE *XC595*

D	Drug	Do mg/m²	Di	V ml	T	R
1,8, 15	nab-Pacliataxel	125	–	–	30'	i.v.
1,8, 15	Gemcitabine	1000	0.9% NaCl	500	30'	i.v.



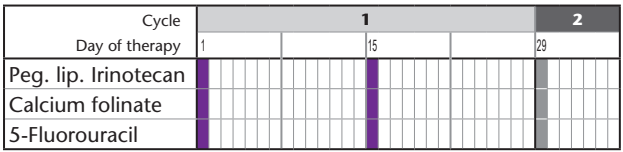
Repetition: Day 29

Number of cycles: 6

Literature:
Von Hoff D.D. et al., N Engl J Med 369: 1691ff, 2013

3.3.5 PEGYLATED LIPOSOMAL IRINOTECAN / 5FU / LEUCOVORIN *XC667*

T	Wirkstoff	D mg/m²	TL	V ml	Z	A
1,15	Pegylated liposomal Irinotecan	70	0.9% NaCl	500	90'	i.v.
1,15	Calcium folinate*	400	0.9% NaCl	250	2h	i.v.
1,15	5-Fluorouracil	2400	0.9% NaCl	500	46h	i.v.



Repetition: Day 29

Number of cycles: 6

Note:

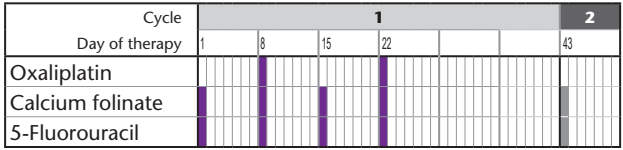
- *Caution:* Irinotecan can lead to life-threatening diarrhea and cholinergic symptoms. Diarrhea can appear either as acute reaction or also some days after Irinotecan administration.
- *Accompanying medication:* Atropine 0.2 mg s.c. or i.v.
- In case of diarrhea: Loperamide initially 4 mg, thereafter 2 mg every 2 hours. Loperamide should be continued for 12 hours following resolution of the diarrhea. If it persists longer than 48 hours, or if there is fever, administration of Ciprofloxacin and hospiatlisation is recommended.
- (*) Calcium folinate as modulator of 5FU should always be administered before 5FU

Literature: Wang-Giliam A. et al., Lancet 387: 545ff, 2016

3.3.6 OXALIPLATIN / LEUCOVORIN / 5FU (OFF)

XC752 (Day 8,22)

D	Drug	Do mg/m²	Di	V ml	T	R
8,22	Oxaliplatin	85	5% Glucose	500	2h	i.v.
1,8, 15, 22	Calcium folinate*	200	0.9% NaCl	250	2h	i.v.
1,8, 15, 22	5-Fluorouracil	2000	0.9% NaCl	1000	24h	i.v.



Repetition: Day 43

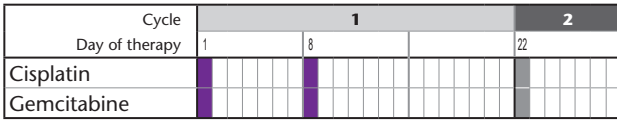
Number of cycles: Until disease progression

Note:
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU.

Literature:
Pelzer U. et al., Onkologie 32: 99ff, 2009

3.3.7 GEMCITABINE / CISPLATIN *XC592*

D	Drug	Do mg/m²	Di	V ml	T	R
1,8	Cisplatin	25	0.9 NaCl	500	1h	i.v.
1,8	Gemcitabine	1000	0.9 NaCl	500	30'	i.v.



Repetition: Day 22

Number of cycles: 8

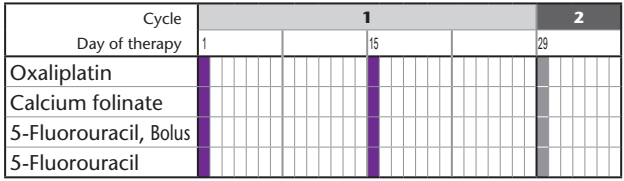
Note:
- Regimen for cholangiocellular carcinomas
- Cisplatin (only if GFR ≥60 ml/ min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min

  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature:
Valle J.W., Br J Cancer 101: 621ff, 2009

3.3.8 Modified FOLFOX-6 *XC588*

D	Drug	Do mg/m²	Di	V ml	T	R
1,15	Oxaliplatin	85	5% Glucose	500	2h	i.v.
1,15	Calcium folinate*	200	0.9% NaCl	250	2h	i.v.
1,15	5-Fluorouracil	400	–	–	Bolus	i.v.
1,15	5-Fluorouracil	2400	0.9% NaCl	500	46h	i.v.



Repetition: Day 29

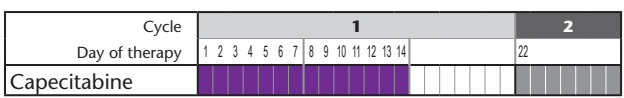
Number of cycles: 6

Note:
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU.

Literature:
Lamarca A. et al., J Clin Oncol 37 (suppl): abstr. 4003

3.3.9 CAPECITABINE *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1-14	Capecitabine	2500	–	–	–	p.o



Repetition: Day 22

Number of cycles: 8

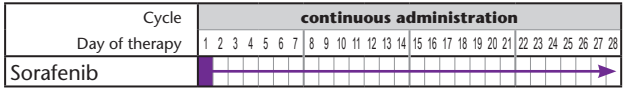
Note:
- 2500 mg/m² divided into 2 equal doses, administered morning and evening within 30 min after a meal.

Literature:
Primrose J.N. et al., Lancet Oncol 20: 663ff, 2019

3.4 Hepatocellular Carcinoma

3.4.1 SORAFENIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Sorafenib	800	–	–	–	p.o.



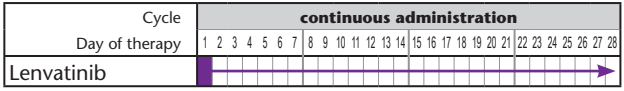
Repetition: * Continuous administration

Note:
- Sorafenib 800 mg divided into 2 equal doses, morning and evening

Literature:
Llovet J.M. et al., N Engl J Med 359: 378ff, 2008

3.4.2 LENVATINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Lenvatinib	12*	–	–	–	p.o.



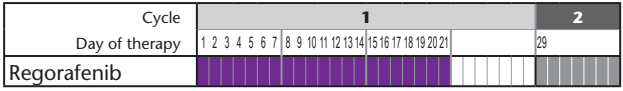
Repetition: * continuous administration

Note:
- (*) Lenvatinib 8 mg/day for patients with < 60kg body weight

Literature:
Kudo M. et al., Lancet 391: 1163ff, 2018

3.4.3 REGORAFENIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-21	Regorafenib	160*	–	–	–	p.o.



Repetition: Day 29

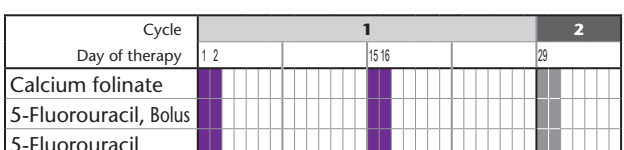
Note:
- (*) 160 mg (4 tablets of 40 mg) taken at once

Literature:
Bruix J. et al., Lancet 389: 56ff, 2017

3.5 Colorectal Cancer

3.5.1 5FU / CALCIUM FOLINATE *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1,2, 15, 16	Calcium folinate*	200	0.9% NaCl	250	2h	i.v.
1,2, 15, 16	5-Fluorouracil	400	–	–	Bolus	i.v.
1,2, 15, 16	5-Fluorouracil	600	0.9% NaCl	500	22h	i.v.



Repetition: Day 29

Number of cycles: 6

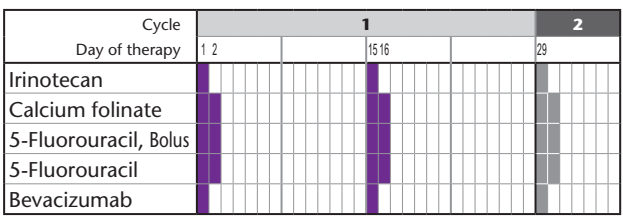
Note:
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU.

Literature:
De Gramont A. et al., J Clin Oncol 15: 808ff, 1997

3.5.2 FOLFIRI + BEVACIZUMAB

XC572 + XA060

D	Drug	Do	Di	V ml	T	R
1,15	Irinotecan	180 mg/m²	0.9% NaCl	500	90'	i.v.
1,2, 15, 16	Calcium folinate*	200 mg/m²	0.9% NaCl	250	2h	i.v.
1,2, 15, 16	5-Fluorouracil	400 mg/m²	–	–	Bolus	i.v.
1,2, 15, 16	5-Fluorouracil	600 mg/m²	0.9% NaCl	500	22h	i.v.
1,15	Bevacizumab	5 mg/kg	0.9% NaCl	100	90'#	i.v.



Repetition: Day 29

Number of cycles: 6
optional: Bevacizumab until progressive disease or for a maximum of 96 weeks

Note:

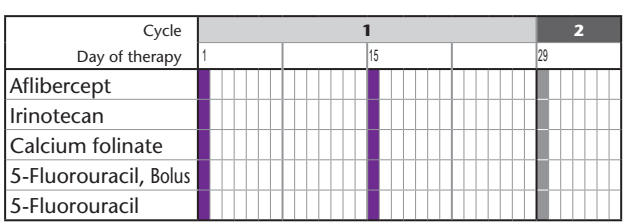
- *Caution:* Irinotecan can lead to life-threatening diarrhea and cholinergic symptoms. Diarrhea can appear either as acute reaction or also some days after Irinotecan administration.
- *Accompanying medication:* Atropine 0.2 mg s.c. or i.v.
- In case of diarrhea: Loperamide initially 4 mg, thereafter 2 mg every 2 hours. Loperamide should be continued for 12 hours following resolution of the diarrhea. If it persists longer than 48 hours, or if there is fever, administration of Ciprofloxacin and hospitalisation is recommended.
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU
- ($^{\#}$) Bevacizumab: The initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.

Literature:

Hurwitz H. et al., N Engl J Med 350: 2335ff, 2004

3.5.3 FOLFIRI + AFLIBERCEPT *XC572 + XA042*

D	Drug	Do	Di	V ml	T	R
1,15	Aflibercept	4 mg/kg	0.9% NaCl	500	1h	i.v.
1,15	Irinotecan	180 mg/m²	0.9% NaCl	500	90'	i.v.
1,15	Calcium folinate*	400 mg/m²	0.9% NaCl	250	2h	i.v.
1,15	5-Fluorouracil	400 mg/m²	–	–	Bolus	i.v.
1,15	5-Fluorouracil	2400 mg/m²	0.9% NaCl	500	46h	i.v.



Repetition: Day 29
Number of cycles: 6

Note:

- *Caution:* Irinotecan can lead to life-threatening diarrhea and cholinergic symptoms. Diarrhea can appear either as acute reaction or also some days after Irinotecan administration.
- *Accompanying medication:* Atropine 0.2 mg s.c. or i.v.
- In case of diarrhea: Loperamide initially 4 mg, thereafter 2 mg every 2 hours. Loperamide should be continued for 12 hours following resolution of the diarrhea. If it persists longer than 48 hours, or if there is fever, administration of Ciprofloxacin and hospitalisation is recommended.
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU
- Aflibercept should be dissolved at 0.6mg/ml to 0.8 mg/ml

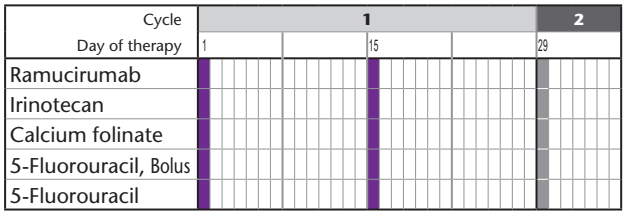
Literature:

Van Cutsem E. et al., J Clin Oncol 30: 3499ff, 2012

3.5.4 FOLFIRI + RAMUCIRUMAB

XC572 + XA088

D	Drug	Do	Di	V ml	T	R
1,15	Ramucirumab	8 mg/kg	0.9% NaCl	250	1h	i.v.
1,15	Irinotecan	180 mg/m²	0.9% NaCl	500	90'	i.v.
1,15	Calcium folinate*	200 mg/m²	0.9% NaCl	250	2h	i.v.
1,15	5-Fluorouracil	400 mg/m²	–	–	Bolus	i.v.
1,15	5-Fluorouracil	2400 mg/m²	0.9% NaCl	500	46h	i.v.



Repetition: Day 29

Number of cycles: 6

Note:

- *Caution:* Irinotecan can lead to life-threatening diarrhea and cholinergic symptoms. Diarrhea can appear either as acute reaction or also some days after Irinotecan administration.
- *Accompanying medication:* Atropine 0.2 mg s.c. or i.v.
- In case of diarrhea: Loperamide initially 4 mg, thereafter 2 mg every 2 hours. Loperamide should be continued for 12 hours following resolution of the diarrhea. If it persists longer than 48 hours, or if there is fever, administration of Ciprofloxacin and hospiatlisation is recommended.
- (*) Calcium folinate as modulator of 5FU should always be administered before 5FU

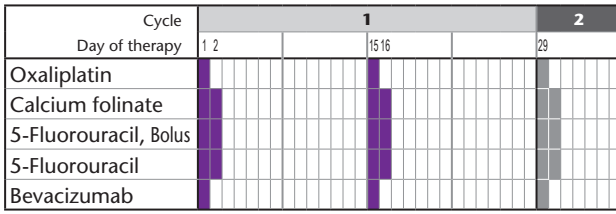
Literature:

Tabernero J. et al., Lancet Oncol 16: 499ff, 2015

3.5.5 FOLFOX-4 + BEVACIZUMAB

XC588 + XA060

D	Drug	Do	Di	V ml	T	R
1,15	Oxaliplatin	85 mg/m²	5% Glucose	500	2h	i.v.
1,2, 15, 16	Calcium folinate*	200 mg/m²	0.9% NaCl	250	2h	i.v.
1,2, 15, 16	5-Fluorouracil	400 mg/m²	–	–	Bolus	i.v.
1,2, 15, 16	5-Fluorouracil	600 mg/m²	0.9% NaCl	500	22h	i.v.
1,15	Bevacizumab	5 mg/kg	0.9% NaCl	100	90'#	i.v.



Repetition: Day 29

Number of cycles: 6

optional: Bevacizumab until progressive disease or intolerability

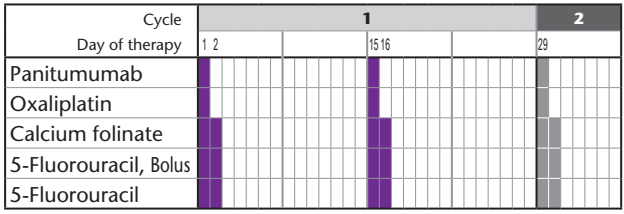
Note:
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU.
- (#) Bevacizumab: The initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.

Literature:
Saltz et al., J Clin Oncol 26: 2013ff, 2008

3.5.6 FOLFOX-4 + PANITUMUMAB

XC588 + XA080

D	Drug	Do	Di	V ml	T	R
1,15	Panitumumab	6 mg/kg	0.9% NaCl	100	1h	i.v.
1,15	Oxaliplatin	85 mg/m²	5% Glucose	500	2h	i.v.
1,2, 15, 16	Calcium folinate*	200 mg/m²	0.9% NaCl	250	2h	i.v.
1,2, 15, 16	5-Fluorouracil	400 mg/m²	–	–	Bolus	i.v.
1,2, 15, 16	5-Fluorouracil	600 mg/m²	0.9% NaCl	500	22h	i.v.



Repetition: Day 29

Number of cycles: 6

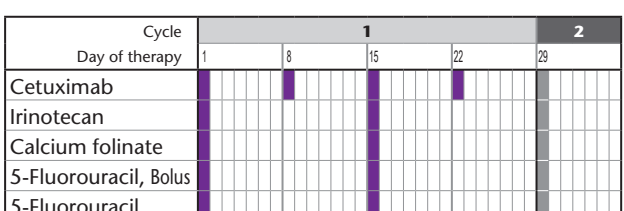
Note:
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU.
- Panitumumab > 1000 mg should be dissolved in 150 ml 0.9% NaCl and administered over 90 min.
  If well tolerated, subsequent doses can be administered over 30 min.

Literature:
Douillard J.Y. et al., J Clin Oncol 28: 4697ff, 2010

3.5.7 FOLFIRI + CETUXIMAB

XC572 + XA070

D	Drug	Do mg/m²	Di	V ml	T	R
1,8, 15, 22	Cetuximab	250#	0.9% NaCl	500	1h	i.v.
1,15	Irinotecan	180	0.9% NaCl	500	90'	i.v.
1,15	Calcium folinate*	400	0.9% NaCl	250	2h	i.v.
1,15	5-Fluorouracil	400	–	–	Bolus	i.v.
1,15	5-Fluorouracil	2400	0.9% NaCl	500	46h	i.v.



Repetition: Day 29

Number of cycles: 6

Note:

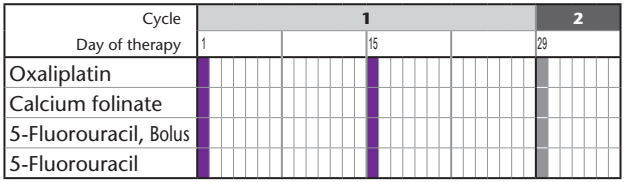
- (*) Calcium folinate as modulator of 5FU should always be administered before 5FU
- (#) Cetuximab: Initial administration over 120 min. at a dose of 400 mg/m^2 before chemotherapy. A one hour gap is mandatory between Cetuximab and other chemotherapeutic agents.
- Optional administration of Cetuximab (500 mg/m^2) in 2-week intervals possible (Yuan et al., JCO 27, 2009 suppl, abstr. e15018)
- *Caution:* Irinotecan can lead to life-threatening diarrhea and cholinergic symptoms. Diarrhea can appear either as acute reaction or also some days after Irinotecan administration
- *Accompanying medication:* Atropine 0.2 mg s.c. or i.v.
- In case of diarrhea: Loperamide initially 4 mg, thereafter 2 mg every 2 hours. Loperamide should be continued for 12 hours following resolution of the diarrhea. If it persists longer than 48 hours, or if there is fever, administration of Ciprofloxacin and hospitalisation is recommended.

Literature:

Van Cutsem E. et al., N Engl J Med 360: 1408ff, 2009

3.5.8 Modified FOLFOX-6 *XC588*

D	Drug	Do mg/m²	Di	V ml	T	R
1,15	Oxaliplatin	85	5% Glucose	500	2h	i.v.
1,15	Calcium folinate*	200	0.9% NaCl	250	2h	i.v.
1,15	5-Fluorouracil	400	–	–	Bolus	i.v.
1,15	5-Fluorouracil	2400	0.9% NaCl	500	46h	i.v.



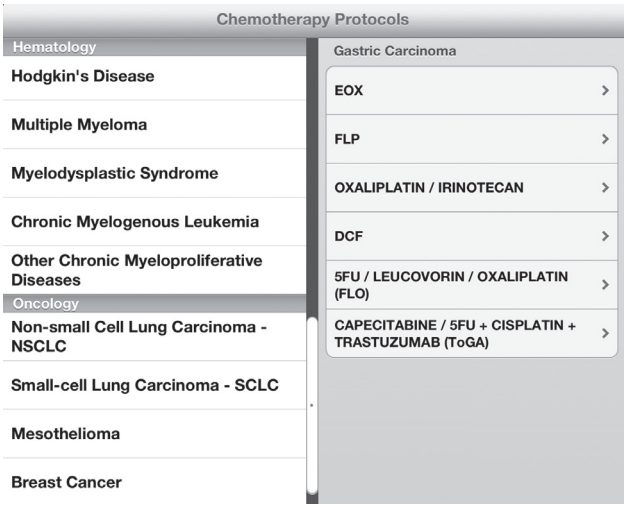
Repetition: Day 29

Number of cycles: 6

Note:
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU.

Literature:
Pectasides D. et al., BMC Cancer 15: 384ff, 2015

Screenshots



D	Drug	Do	Di	V	T	R
1	Rituximab	375 mg/m²	0.9% NaCl	500 ml	5h (3h)	i.v.
1,2	Bendamustine	90 mg/m²	0.9% NaCl	500 ml	30'	i.v.

Repetition: Day 29

Comments

- Rituximab: Recommended infusion rate at the initial infusion: 50 mg/h during the first 30 min. thereafter increase infusion rate by 50 mg/h every 30 min (highest rate: 400 mg/h). Additional infusions can be started with 100 mg/h and increased by 100 mg/h every 30 min. (highest rate: 400 mg/h). Premedication with 30 mg Diphenhydramine is recommended.

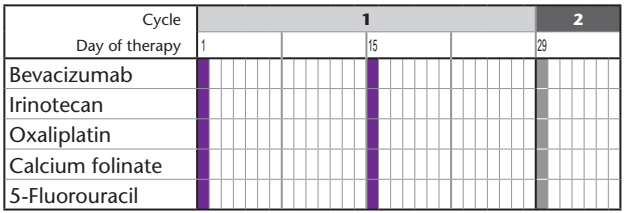
Literature

Rummel M.J. et al., J Clin Oncol 23: 3383ff, 2008

3.5.9 FOLFOXIRI + BEVACIZUMAB

XC578+XA060

D	Drug	Do	Di	V ml	T	R
1,15	Bevacizumab*	5 mg/kg	0.9% NaCl	100	1h	i.v.
1,15	Irinotecan	165 mg/m²	0.9% NaCl	500	1h	i.v.
1,15	Oxaliplatin	85 mg/m²	5% Glucose	500	2h	i.v.
1,15	Calcium folinate#	200 mg/m²	0.9% NaCl	250	2h	i.v.
1,15	5-Fluorouracil	3200 mg/m²	0.9% NaCl	1000	48h	i.v.



Repetition: Day 29

Number of cycles: 6
optional: Bevacizumab until progressive disease or intolerability

Note:

- (*) Bevacizumab: The initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min. If the 60minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.
- *Caution:* Irinotecan can lead to life-threatening diarrhea and cholinergic symptoms. Diarrhea can appear either as acute reaction or also some days after Irinotecan administration.
- *Accompanying medication:* Atropine 0.2 mg s.c. or i.v.
- In case of diarrhea: Loperamide initially 4 mg, thereafter 2 mg every 2 hours. Loperamide should be continued for 12 hours following resolution of the diarrhea. If it persists longer than 48 hours, or if there is fever, administration of Ciprofloxacin and hospiatlisation is recommended.
- ($^{\#}$) Calcium folinate as modulator of 5FU should always be administered before 5FU

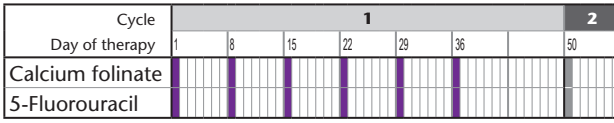
Literature:

Cremolini C. et al., Lancet Oncol 16: 1306ff, 2015

3.5.10 HD 5FU (modified according to Ardalan)

XA149

D	Drug	Do mg/m²	Di	V ml	T	R
1,8, 15, 22, 29, 36	Calcium folinate*	500	0.9% NaCl	250	2h	i.v.
1,8, 15, 22, 29, 36	5-Fluorouracil	2600	0.9% NaCl	1000	22h	i.v.



Repetition: Day 50

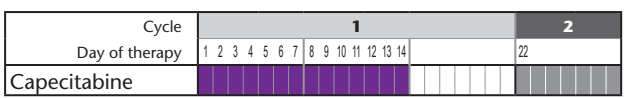
Number of cycles: Until progressive disease or intolerability

Note:
- (*) Calcium folinate as a modulator of 5FU should always be administered before 5FU.

Literature:
Weh H.J. et al., Ann Oncol 5: 233ff, 1994

3.5.11 CAPECITABINE *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1-14	Capecitabine	2500	–	–	–	p.o



Repetition: Day 22

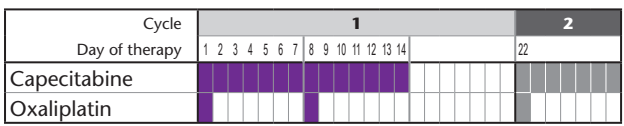
Number of cycles: Until progressive disease or intolerability

Note:
- 2500 mg/m² divided into 2 equal doses, administered morning and evening within 30 min after a meal.

Literature:
Twelves C. et al., Eur J Cancer 37: 597ff, 2001

3.5.12 CAPECITABINE / OXALIPLATIN *XC752*

D	Drug	Do mg/m²	Di	V ml	T	R
1-14	Capecitabine	2000	–	–	–	p.o.
1,8	Oxaliplatin	70	5% Glucose	500	2h	i.v.



Repetition: Day 22

Number of cycles: 6

Note:
- Capecitabine 2000 mg/m² divided into 2 equal doses, administered morning and evening within 30 min after a meal.
- In the adjuvant setting, Oxaliplatin will be administered at a dose of 130 mg/m² on day 1 (repetition: d22), while the dose and schedule of Capecitabine will be maintained at 2000 mg/m². (No of cycles: 8).
  (Haller D. et al., J Clin Oncol 29: 1465ff, 2011)

Literature:
Porschen R. et al., J Clin Oncol 25: 421ff, 2007

3.5.13 RALTITREXED *XC812*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Raltitrexed	3	0.9% NaCl	100	15'	i.v.

Cycle	1	2
Day of therapy	1	22
Raltitrexed		

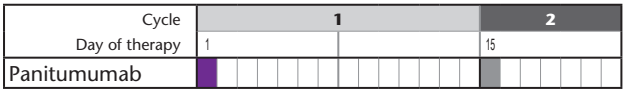
Repetition: Day 22

Number of cycles: 6

Literature:
Cunnigham D. et al., Eur J Cancer, 31A: 1945ff, 1995

3.5.14 PANITUMUMAB *XA080*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Panitumumab	6	0.9% NaCl	100	1h	i.v.



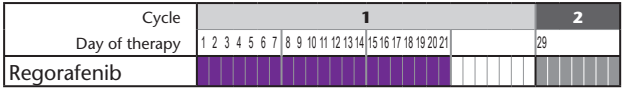
Repetition: Day 15

Note:
- Panitumumab >1000 mg should be dissolved in 150 ml of 0.9% NaCl and administered over 90 min.

Literature:
Van Cutsem E. et al., J Clin Oncol 25: 1658ff, 2007

3.5.15 REGORAFENIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-21	Regorafenib	160*	–	–	–	p.o.



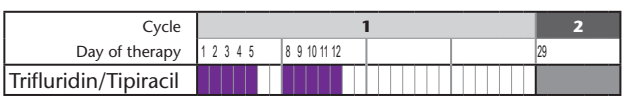
Repetition: Day 29

Note:
- (*) 160 mg (4 tablets of 40 mg) taken at once

Literature:
Grothey A. et al., Lancet 381: 303ff, 2013

3.5.16 TRIFLURIDINE / TIPIRACIL *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1-5, 8-12	Trifluridine/Tipiracil	70	–	–	–	p.o.



Repetition: Day 29

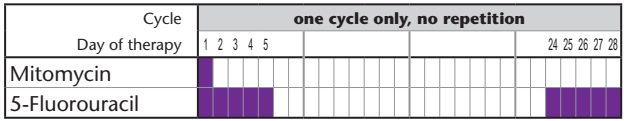
Note:
- Trifluridine/Tipiracil: 70 mg/m² divided into 2 equal doses, morning and evening.

Literature:
Mayer R.J. et al., N Engl J Med 372: 1909ff, 2015

3.6 Anal Cancer

3.6.1 MITOMYCIN / 5FU + RT *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Mitomycin	12	–	–	Bolus	i.v.
1-5, 24-28	5-Fluorouracil	750	0.9% NaCl	1000	24h	i.v.



Repetition: None

Number of cycles: Until progressive disease or intolerability

Note:
- 5FU by continuous infusion during the first and final weeks of radiotherapy

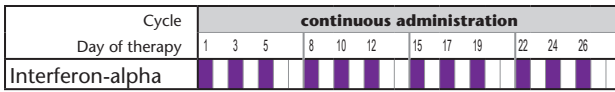
Literature:

UKCCCR Anal Cancer Trial Working Party, Lancet 348: 1049ff, 1996
Bartelink H. et al., J Clin Oncol 15: 2040ff, 1997

3.7 Neuroendocrine Tumor/Cancer

3.7.1 INTERFERON ALPHA *XA149*

D	Drug	Do IU	Di	V ml	T	R
3x/wk	Interferon-alpha	5 Mio.	–	–	–	s.c.



Repetition: Continuous administration

Note:
- 500 mg Paracetamol 30 min before administration of Interferon alpha

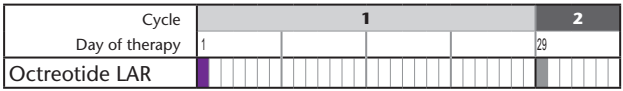
Literature:
Öberg K. et al., Acta Oncol 30: 519ff, 1991

3.7.2 LANREOTIDE or OCTREOTIDE *XA149*

D	Drug	Do mg	Di	V ml	T	R
1	Lanreotide LAR	120	–	–	–	s.c.

Alternatively

D	Drug	Do mg	Di	V ml	T	R
1	Octreotide LAR	30	–	–	–	s.c.



Repetition: Day 29

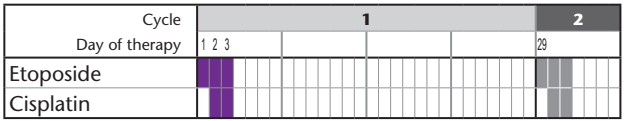
Number of cycles: Until progressive disease or intolerability

Note:
- Alternatively: Octreotid 0.2 mg s.c. tid

Literature:
Caplin M.E. et al., N Engl J Med 371: 224ff, 2014
Öberg K. et al., Acta Oncol 15: 966ff, 2004

3.7.3 ETOPOSIDE / CISPLATIN *XC304*

D	Drug	Do mg/m²	Di	V ml	T	R
1, 2,3	Etoposide	130	0.9% NaCl	1000	24h	i.v.
2,3	Cisplatin	45	0.9% NaCl	1000	24h	i.v.



Repetition: Day 29

Number of cycles: 6

Note:
- Etoposide should be dissolved in 1000 ml 0.9% NaCl if total dose is ≥ 200 mg.
- Cisplatin (only if ≥GFR 60 ml/ min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature:
Moertel C.G. et al., Cancer 68: 227ff, 1991

3.7.4 DOXORUBICIN *XC444*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Doxorubicin	60	0.9% NaCl	250	1h	i.v.

Cycle	1	2
Day of therapy	1	22 (29)
Doxorubicin		

Repetition: Day 22 (29)

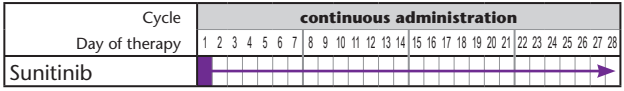
Number of cycles: 6

Note:
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative dose ≥500 mg/m²

Literature:
Engstrom P. et al., J Clin Oncol 2: 1255ff, 1984

3.7.5 SUNITINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Sunitinib	37.5	–	–	–	p.o.



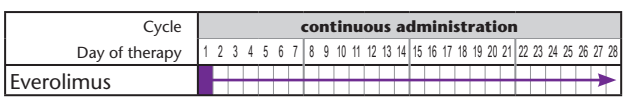
Repetition: * Continuous administration

Note:
- *Caution:* Hypothyroidism
- Approval for pancreatic NETs only

Literature:
Raymond E. et al., N Engl J Med 364: 501ff, 2011

3.7.6 EVEROLIMUS *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Everolimus	10	–	–	–	p.o.



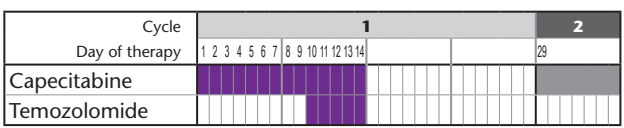
Repetition: * Continuous administration

Note:
- 10 mg at once (2 x 5 mg)

Literature:
Yao J.C. et al., N Engl J Med 364: 514ff, 2011
Yao J.C. et al., Lancet 387: 968ff, 2016

3.7.7 CAPECITABINE / TEMOZOLOMIDE *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1-14	Capecitabine	1500	–	–	–	p.o.
10-14	Temozolomide	200	–	–	–	p.o.



Repetition: Day 29

Number of cycles: 6

Note:
- Capecitabine: 1500 mg/m² divided into 2 equal doses, morning and evening within 30 min after a meal.

Literature:
Ramirez R.A. et al., The Oncologist 21: 671ff, 2016

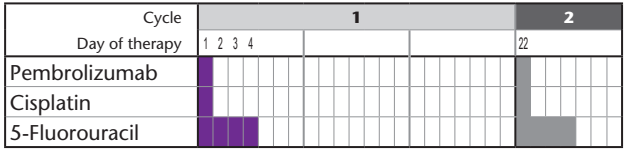
Chapter 4

Head and Neck Cancer

4.1 CISPLATIN / 5FU + PEMBROLIZUMAB

XC284 + XA081

D	Drug	Do	Di	V ml	T	R
1	Pembrolizumab	200 mg	0.9% NaCl	100	30'	i.v.
1	Cisplatin	100 mg/m²	0.9% NaCl	1000	1h	i.v.
1-4	5-Fluorouracil	1000 mg/m²	0.9% NaCl	1000	22h	i.v.



Repetition: Day 22

Number of cycles: Cisplatin/5FU: 6;
Pembrolizumab: for up to 35

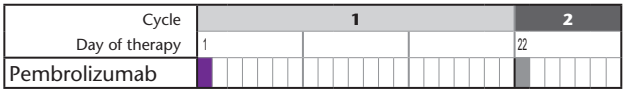
Note:

- Pembrolizumab should be dissolved at 1-10 mg/ml
- Cisplatin (only if GFR ≥60 ml/min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl
- In case of Carboplatin (AUC 5) administration: XC196 (d1)

Literature: Burtness B. et al., Lancet 394: 1915ff, 2019

4.2 PEMBROLIZUMAB *XA081*

D	Drug	Do mg	Di	V ml	T	R
1	Pembrolizumab	200	0.9% NaCl	100	30'	i.v.



Repetition: Day 22

Number of cycles: Until progressive disease or intolerability

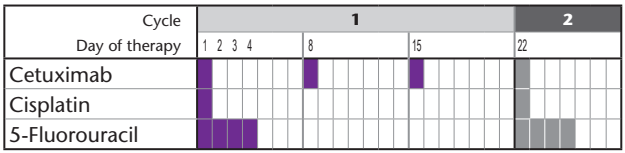
Note:
- Pembrolizumab should be dissolved at 1-10 mg/ml

Literature:
Burtness B. et al., Lancet 394: 1915ff; 2019

4.3 CISPLATIN / 5FU + CETUXIMAB

XA284 + XA070 (Day 1), XA070 (Day 8,15)

D	Drug	Do mg/m²	Di	V ml	T	R
1,8, 15	Cetuximab	250*	0.9% NaCl	500	1h	i.v.
1	Cisplatin	100	0.9% NaCl	1000	1h	i.v.
1-4	5-Fluorouracil	1000	0.9% NaCl	1000	22h	i.v.



Repetition: Day 22

Number of cycles: 6

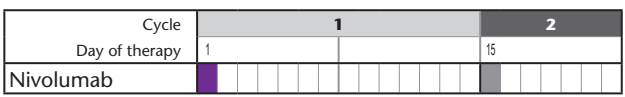
Note:

- Cisplatin (only if GFR ≥60 ml/min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl
- (*) Cetuximab: initial administration over 120 min. If well tolerated, subsequent doses can be administered over 60 min. A one hour gap is mandatory between Cetuximab and other chemotherapeutic agents

Literature: Vermorken J.B. et al., N Engl J Med 359: 1116ff, 2008

4.4 NIVOLUMAB *XA085*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Nivolumab*	3	0.9% NaCl	100	1h	i.v.



Repetition: Day 15

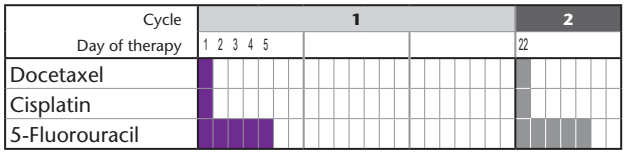
Number of cycles: Until progressive disease or intolerability

Note:
- Nivolumab should be dissolved at 1-10 mg/ml
- (*) Nivolumab can also be administered at 240 mg flat-dose every 2 weeks (Zhao X. et al., Ann Oncol 28: 2002ff, 2017) or at 480mg every 4 weeks (Long G.V. et al.; Ann Oncol 29: 2208ff, 2018)

Literature:
Ferris R.L. et al., N Engl J Med 375: 1856ff, 2016

4.5 DCF *XC412*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Docetaxel	75	0.9% NaCl	250	1h	i.v.
1	Cisplatin	75	0.9% NaCl	1000	2h	i.v.
1-5	5-Fluorouracil	750	0.9% NaCl	1000	24h	i.v.



Repetition: Day 22

Note:
- Docetaxel should be dissolved at 0.3 - 0.74 mg/ml
- *Accompanying medication:*
  Dexamethasone 8 mg orally 2x daily for 3 days starting one day before Docetaxel administration
- Cisplatin (only if GFR ≥60 ml/min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

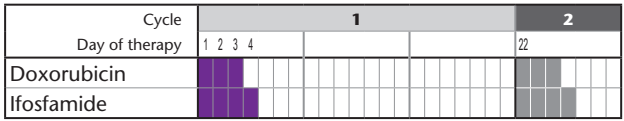
Literature:
Vermorken J.B. et al., N Engl J Med 357: 1695ff, 2007

Chapter 5

Soft Tissue Sarcoma

5.1 DOXORUBICIN / IFOSFAMIDE *XC448*

D	Drug	Do mg/m²	Di	V ml	T	R
1-3	Doxorubicin	25	0.9% NaCl	250	1h	i.v.
1-4	Ifosfamide	2500	0.9% NaCl	500	23h	i.v.



Repetition: Day 22

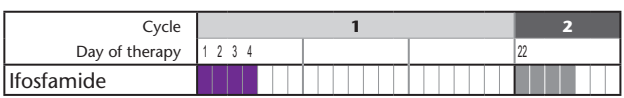
Number of cycles: 6

Note:
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative doses ≥500 mg/m²
- *Mesna continuous infusion:* Dose (as an i.v. bolus) is equal to 20% of the Ifosfamide dose, followed by a continuous infusion of mesna at 40% of the Ifosfamide dose, continue mesna infusion 12-24 hours after completion of Ifosfamide infusion.

Literature:
Judson I. et al., Lancet Oncol 15: 415ff, 2014

5.2 IFOSFAMIDE *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1-4	Ifosfamide	2000	0.9% NaCl	500	24h	i.v.



Repetition: Day 22

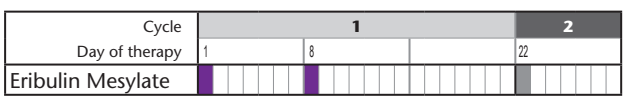
Number of cycles: 6

Note:
- *Mesna continuous infusion:* Dose (as an i.v. bolus) is equal to 20% of the Ifosfamide dose, followed by a continuous infusion of mesna at 40% of the Ifosfamide dose, continue mesna infusion 12-24 hours after completion of Ifosfamide infusion.
- Increased risk of CNS toxicity if albumin ≤3.5 g/dl

Literature:
Antman K.H. et al., J Clin Oncol 7: 126ff, 1989

5.3 ERIBULIN MESYLATE *XC494*

D	Drug	Do mg/m²	Di	V ml	T	R
1,8	Eribulin Mesylate*	1.4	0.9% NaCl	100	2-5'	i.v.



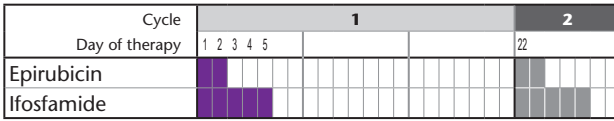
Repetition: Day 22

Note:
- (*) equivalent Eribulin dose of 1.23 mg/m² d1,8

Literature:
Schöffski P. et al., Lancet 387: 1629ff, 2016

5.4 EPIRUBICIN / IFOSFAMIDE *XC476*

D	Drug	Do mg/m²	Di	V ml	T	R
1,2	Epirubicin	60	0.9% NaCl	500	1h	i.v.
1-5	Ifosfamide	1800	0.9% NaCl	500	1h	i.v.



Repetition: Day 22

Number of cycles: 5

Note:

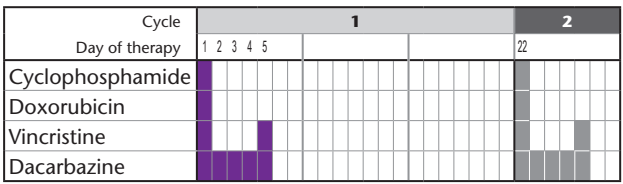
- *Caution:* Cardiac toxicity of Epirubicin at cumulative doses ≥1000 mg/m²
- *Mesna:* Dose is equal to 100% of the Ifosfamide dose, given as 20% of the Ifosfamide dose i.v. at hour 0, followed by 40% of the Ifosfamide dose given orally 2- and 6 hours after start of Ifosfamide
- Increased risk of CNS toxicity if albumin ≤3.5 g/dl

Literature:

Frustaci S et al., J Clin Oncol 19: 1238ff, 2001

5.5 CYVADIC (EORTC) *XC376*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Cyclophosphamide	500	0.9% NaCl	250	1h	i.v.
1	Doxorubicin	50	0.9% NaCl	250	1h	i.v.
1,5	Vincristine	1*	0.9% NaCl	100	10'	i.v.
1-5	Dacarbazine	250	0.9% NaCl	500	1h	i.v.



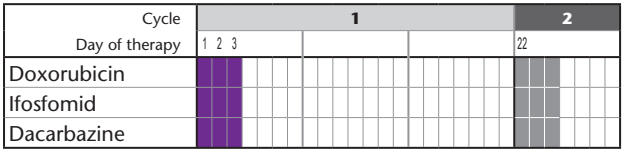
Repetition: Day 22
Number of cycles: 6
Note:

- *Mesna:* Dose is equal to 100% of the Ifosfamide dose, given as 20% of the Ifosfamide dose i.v. at hour 0, followed by 40% of the Ifosfamide dose given orally 2- and 6 hours after start of Ifosfamide
- (*) Vincristine max. 2 mg
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative doses ≥500 mg/m²
- Dacarbazine: light-resistent infusion set mandatory

Literature: Gottlieb J.A. et al., Cancer Chemother Res 58: 265ff, 1974

5.6 MAID *XC444*

D	Drug	Do mg/m²	Di	V ml	T	R
1-3	Doxorubicin	20	0.9% NaCl	500	24h	i.v.
1-3	Ifosfamide	2500	0.9% NaCl	1000	24h	i.v.
1-3	Dacarbazine	300	0.9% NaCl	500	24h	i.v.



Repetition: Day 22

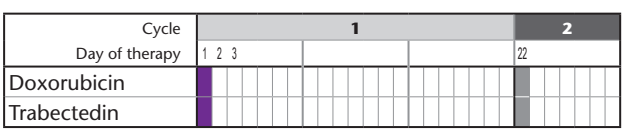
Number of cycles: 6

Note:
- *Mesna continuous infusion:* Dose (as an i.v. bolus) is equal to 20% of the Ifosfamide dose, followed by a continuous infusion of mesna at 40% of the Ifosfamide dose, continue mesna infusion 12-24 hours after completion of Ifosfamide infusion.
- Increased risk of CNS-toxicity if albumin ≤3.5 g/dl
- *Caution:* Cardiac toxicity of Doxorubicin at cumulative doses ≥500 mg/m²
- Dacarbazine: light-resistant infusion set mandatory

Literature:
Elias A. et al., J Clin Oncol 7: 1208ff, 1989

5.7 DOXORUBICIN / TRABECTEDIN *XC954*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Doxorubicin	60	0.9% NaCl	250	1h	i.v.
1	Trabectedin	1.1	0.9% NaCl	1000	24h*	i.v.



Repetition: Day 22

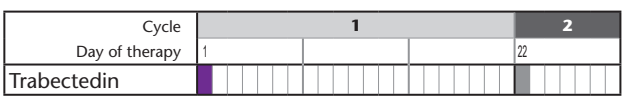
Number of cycles: 6

Note:
- In the presence of a central venous device, Trabectedin can also be dissolved in 500 ml 0.9% NaCl and be administered over 3h

Literature:
Pautier P. et al., Lancet Oncol 16: 457ff, 2015

5.8 TRABECTEDIN *XC952*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Trabectedin	1.5	0.9% NaCl	1000	24h	i.v.



Repetition: Day 22

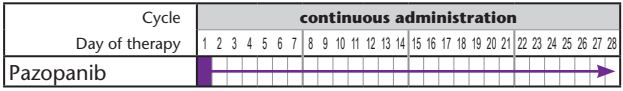
Number of cycles: *6*

Note:
- In the presence of a central venous device, Trabectedin can also be dissolved in 500 ml 0.9 % NaCl

Literature:
Demetri G.D. et al., J Clin Oncol 27: 4188ff, 2009

5.9 PAZOPANIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Pazopanib	800	–	–	–	p.o.



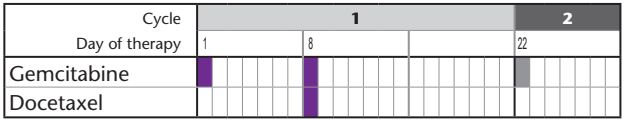
Repetition: * Continuous administration

Literature:

Van der Graaf W.T., Lancet 379: 1879ff, 2012

5.10 GEMCITABINE / DOCETAXEL *XC416*

D	Drug	Do mg/m²	Di	V ml	T	R
1,8	Gemcitabine	900	0.9 NaCl	500	30'	i.v.
8	Docetaxel	100	0.9 NaCl	250	1h	i.v.



Repetition: Day 22

Note:
- Docetaxel should be dissolved at 0.3-0.74 mg/ml
- *Accompanying medication:* Dexamethasone 8 mg orally 2x daily for 3 days starting one day before docetaxel administration

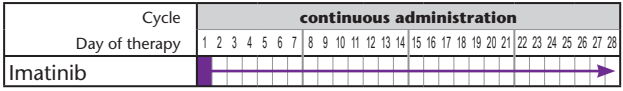
Literature:
Maki R.G. at al., J Clin Oncol 25: 2755ff, 2007

Chapter 6

Gastrointestinal Stromal Tumors

6.1 IMATINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Imatinib	400	–	–	–	p.o.

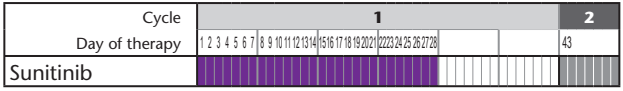


Repetition: * Continuous administration

Literature:
Demetri G.D. et al., N Engl J Med 347: 472ff, 2002

6.2 SUNITINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-28	Sunitinib	50	–	–	–	p.o.



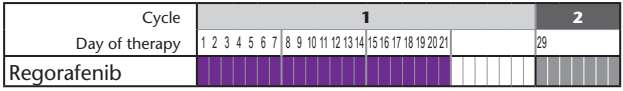
Repetition: Day 43

Note:
- *Caution:* Hypothyroidism
- Sunitinib can also be administered continuously at a daily dose of 37.5 mg (George S. et al., J Clin Oncol 27: 3154ff, 2009)

Literature:
Demetri G.D. et al., Lancet 368: 1329ff, 2006

6.3 REGORAFENIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-21	Regorafenib	160*	–	–	–	p.o.



Repetition: Day 29

Note:
- (*) 160 mg (4 tablets of 40 mg) taken at once

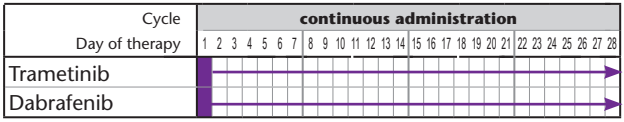
Literature:
Demetri G.D. et al., Lancet 381: 295ff, 2013

Chapter 7

Melanoma

7.1 TRAMETINIB / DABRAFENIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Trametinib	2	–	–	–	p.o.
1-*	Dabrafenib	300#	–	–	–	p.o.



Repetition: * Continuous administration

Note:
- (#) Dabrafenib 150 mg twice daily
- In the adjuvant setting patients are treated for 12 months

Literature:
Long G.V. et al., Lancet 386: 444ff, 2015
Robert C. et al., N Engl J Med 372: 30ff, 2015
Long G.V. et al., N Engl J Med 377: 1813ff, 2017

7.2 PEMBROLIZUMAB *XA081*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Pembrolizumab	2	0.9 NaCl	100	30'	i.v.

Cycle	1	2
Day of therapy	1	22
Pembrolizumab		

Repetition: Day 22

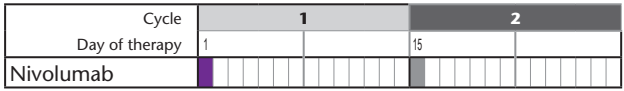
Number of cycles: Until progressive disease or intolerability

Note:
- Pembrolizumab should be dissolved at 1 - 10 mg/ml

Literature:
Ribas A. et al., Lancet Oncol 16: 908ff, 2015
Eggermont A.M.M. et al., N Engl J Med 378: 1789ff; 2018

7.3 NIVOLUMAB *XA085*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Nivolumab*	3	0.9 NaCl	100	1h	i.v.



Repetition: Day 15

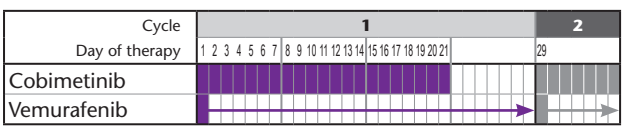
Number of cycles: Until progressive disease or intolerability

Note:
- Nivolumab should be dissolved at 1 - 10 mg/ml
- In the adjuvant setting patients are treated for 12 months
- (*) Nivolumab can also be administered at 240 mg flat-dose every 2 weeks (Zhao X. et al., Ann Oncol 28: 2002ff, 2017) or at 480 mg every 4 weeks (Long G.V. et al.; Ann Oncol 29: 2208ff, 2018)

Literature:
Weber J.S. et al., Lancet Oncol. 16: 375ff, 2015
Robert C. et al. N Engl J Med 372: 320ff, 2015
Weber J. et al., N Engl J Med 377: 1824ff, 2017

7.4 COBIMETINIB / VEMURAFENIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-21	Cobimetinib	60	–	–	–	p.o.
1-*	Vemurafenib	1920#	–	–	–	p.o.



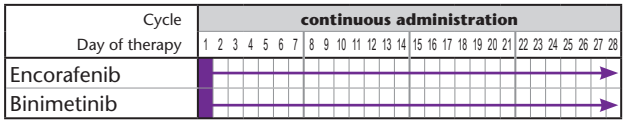
Repetition: Day 29, * continuous administration

Note:
- (#) Vemurafenib 960 mg twice daily

Literature:
Larkin J. et al., N Engl J Med 371: 1867ff, 2014

7.5 ENCORAFENIB / BINIMETINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Encorafenib	450	–	–	–	p.o.
1-*	Binimetinib	90*	–	–	–	p.o.



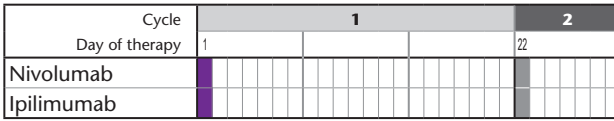
Repetition: * Continuous administration

Note:
- (*) Binimetinib: 90 mg divided into 2 equal doses, morning and evening.

Literature:
Dummer R. et al., Lancet Oncol 19: 603ff, 2018

7.6 IPILIMUMAB / NIVOLUMAB *XA084 + XA085*

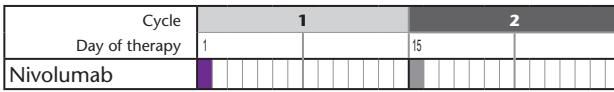
D	Drug	Do mg/kg	Di	V ml	T	R
1	Nivolumab*	1	0.9 NaCl	100	1h	i.v.
1	Ipilimumab	3	0.9 NaCl	100	90'	i.v.



Repetition: Day 22

Number of cycles: 1-4

D	Drug	Do mg/kg	Di	V ml	T	R
1	Nivolumab	3	0.9 NaCl	100	1h	i.v.



Repetition: Day 15

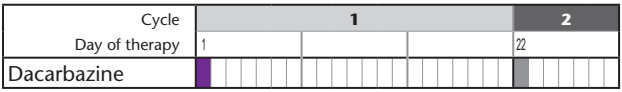
Number of cycles: From cycle 5 onwards until progressive disease or intolerability

Note:
- Nivolumab should be dissolved at 1 - 10 mg/ml
- (*) Nivolumab can also be administered at 240 mg flat-dose every 2 weeks (Zhao X. et al., Ann Oncol 28: 2002ff, 2017) or at 480 mg every 4 weeks (Long G.V. et al.; Ann Oncol 29: 2208ff, 2018)
- Ipilimumab should be dissolved at 1 - 4 mg/ml

Literature:
Larkin J. et al., N Engl J Med 373: 23ff, 2015
Postow M.A. et al., N Engl J Med 372: 2006ff, 2015

7.7 DACARBAZINE *XA149*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Dacarbazine	1000	0.9% NaCl	500	2h	i.v.



Repetition: Day 22

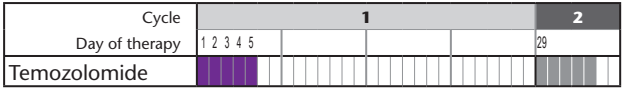
Number of cycles: 6

Note:
- *Caution:* light-resistant infusion set mandatory

Literature:
Chapman P.B. et al., J Clin Oncol 17: 2745ff, 1999

7.8 TEMOZOLOMIDE *XC820*

D	Drug	Do mg/m²	Di	V ml	T	R
1-5	Temozolomide	200	–	–	–	p.o.



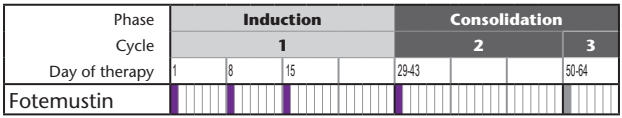
Repetition: Day 29

Number of cycles: 6

Literature:
Middleton M.R. et al., J Clin Oncol 18: 158ff, 2000

7.9 FOTEMUSTIN *XC564*

D	Drug	Do mg/m²	Di	V ml	T	R
1,8, 15	Fotemustin	100	5% Glucose	500	1h	i.v.



Repetition: Day 29-43

Number of cycles: Until progressive disease or intolerability

Note:
- Subsequent to the induction phase (Day 1,8,15) the consolidation phase is to be initiated (Start: Day 29-43), Fotemustin 100 mg/m² is to be administered only once every three weeks.
- Fotemustin should not be stored for more than 4 hours at room temperature
  (*Caution:* Strict protection from light is required).

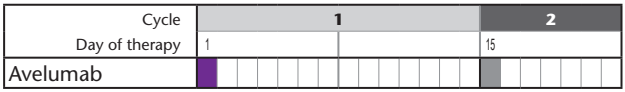
Literature:
Jacquillat C. et al., Cancer 66: 1873ff, 1990

Chapter 8

Merkel Cell Carcinoma

8.1 AVELUMAB *XA056*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Avelumab	10	0.9% NaCl	250	1h	i.v.



Repetition: Day 15

Number of cycles: Until progressive disease or intolerability

Literature:
Kaufmann H.L. et al., Lancet Oncol 17: 1374ff, 2016

Chapter 9

Thyroid Cancer

9.1 VANDETANIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Vandetanib	300	–	–	–	p.o.

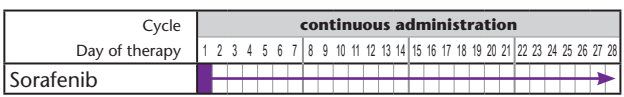
Cycle	continuous administration
Day of therapy	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
Vandetanib	

Repetition: * Continuous administration

Literature:
Wells S.A. et al., J Clin Oncol 30: 134ff, 2011

9.2 SORAFENIB

D	Drug	Do mg	Di	V ml	T	R
1-*	Sorafenib	800#	–	–	–	p.o.



Repetition: * Continuous administration

Note:

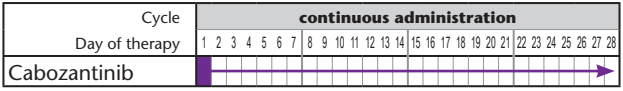
- (#) 800 mg divided into two equal doses, morning and evening

Literature:

Brose M.S. et al., Lancet 384: 319ff, 2014

9.3 CABOZANTINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Cabozantinib	140#	–	–	–	p.o.



Repetition: * Continuous administration

Note:

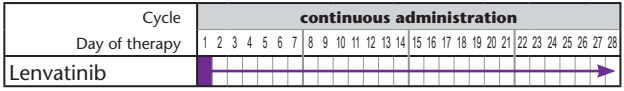
- (#) 140 mg (one 80 mg capsule and 3 x 20 capsule) taken at once

Literature:

Elisei R. et al., J Clin Oncol 31: 3639ff, 2013

9.4 LENVATINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Lenvatinib	24#	–	–	–	p.o.



Repetition: * Continuous administration

Note:

- (#) 24 mg (two 10 mg capsules and one 4 mg capsule) taken once daily

Literature:

Schlumberger M. et al., N Engl J Med 372: 621ff, 2015

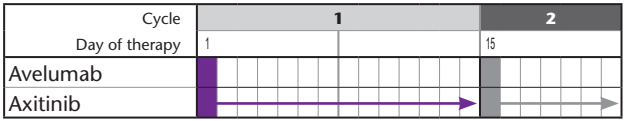
Chapter 10

Tumors of the Urogenital Tract

10.1 Renal Cell Carcinoma

10.1.1 AVELUMAB + AXITINIB *XA056*

D	Drug	Do	Di	V ml	T	R
1	Avelumab	10 mg/kg	0.9% NaCl	250	1h	i.v.
1-*	Axitinib	10 mg[#]	–	–	–	p.o.



Repetition: Avelumab d15,
* continuous administration

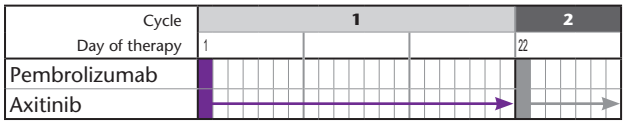
Number of cycles: Until progressive disease or intolerability

Note:
- ([#]) Axitinib 10mg divided into 2 equal doses, morning and evening.

Literature:
Motzer R.J. et al., N Engl J Med 380: 1103ff, 2019

10.1.2 PEMBROLIZUMAB + AXITINIB *XA081*

D	Drug	Do	Di	V ml	T	R
1	Pembrolizumab	200 mg	0.9% NaCl	100	30'	i.v.
1-*	Axitinib	10 mg#	–	–	–	p.o.



Repetition: Pembrolizumab d22,
* continuous administration

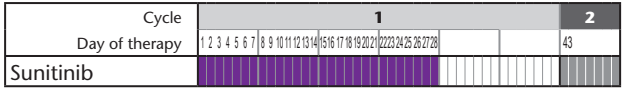
Number of cycles: Until progressive disease or intolerability

Note:
- Pembrolizumab should be dissolved at 1-10 mg/ml
- (#) Axitinib 10 mg divided into 2 equal doses, morning and evening

Literature:
Rini B.I. et al., N Engl J Med 380: 1116ff, 2019

10.1.3 SUNITINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-28	Sunitinib	50	–	–	–	p.o.



Repetition: Day 43

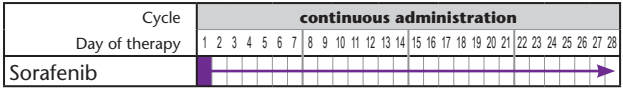
Number of cycles: Until progressive disease or intolerability

Note:
- *Caution:* Hypothyroidism
- Sunitinib can also be administered continuously at a daily dose of 37.5 mg
  (Escudier B. et al., J Clin Oncol 27: 4068ff, 2009).

Literature:
Motzer R.J. et al., N Engl J Med 356: 115ff, 2007
Motzer R.J. et al., J Clin Oncol 27: 3584ff, 2009

10.1.4 SORAFENIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Sorafenib	800	–	–	–	p.o.



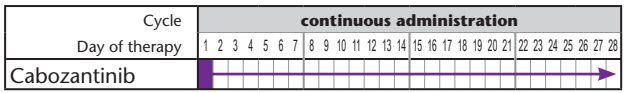
Repetition: * Continuous administration

Note:
- 800 mg divided into 2 equal doses, morning and evening

Literature:
Escudier B. et al., N Engl J Med 356: 125ff, 2007

10.1.5 CABOZANTINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Cabozantinib	60#	–	–	–	p.o.



Repetition: * Continuous administration

Note:

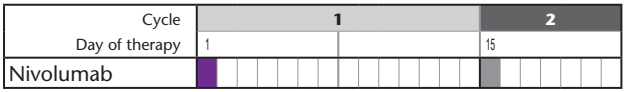
- (#) 60 mg (three 20 mg capsules) taken at once

Literature:

Choueiri T.K. et al., N Engl J Med 373: 1814ff, 2015

10.1.6 NIVOLUMAB *XA085*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Nivolumab*	3	0.9% NaCl	100	1h	i.v.



Repetition: Day 15

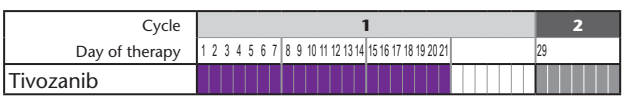
Number of cycles: Until progressive disease or intolerability

Note:
- Nivolumab should be dissolved at 1 - 10 mg/ml
- (*) Nivolumab can also be administered at 240 mg flat-dose every 2 weeks (Zhao X. et al., Ann Oncol 28: 2002ff, 2017) or at 480 mg every 4 weeks (Long G.V. et al.; Ann Oncol 29: 2208ff, 2018)

Literature:
Motzer R.J. et al., N Engl J Med 373: 1803ff, 2015

10.1.7 TIVOZANIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-21	Tivozanib	1.5	–	–	–	p.o.

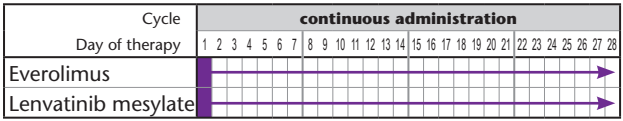


Repetition: Day 29

Literature:
Motzer R.J. et al., J Clin Oncol 31: 3791ff, 2013

10.1.8 EVEROLIMUS / LENVATINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Everolimus	5	–	–	–	p.o.
1-*	Lenvatinib mesylate	18	–	–	–	p.o.

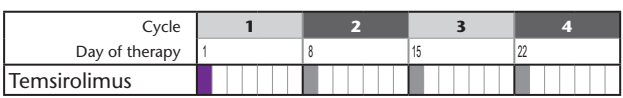


Repetition: * Continuous administration

Literature:
Motzer R.J. et al., Lancet Oncol 16: 1473ff, 2015

10.1.9 TEMSIROLIMUS *XA030*

D	Drug	Do mg	Di	V ml	T	R
1	Temsirolimus	25	0.9% NaCl	250	1h	i.v.



Repetition: Day 8

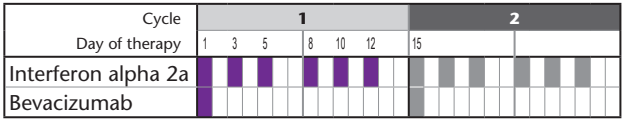
Note:
- *Accompanying medication:*
  Premedication with 30 mg Diphenhydramine is optional
- Administration has to be performed via a light-protected PVC-free infusion device and Inline-filter.

Literature:
Hudes G. et al., N Engl J Med 356: 2271ff, 2007

10.1.10 INTERFERON ALPHA + BEVACIZUMAB

XA149 + XA060

D	Drug	Do	Di	V ml	T	R
1,3, 5,8, 10, 12	Interferon alpha 2a	3 MIU (absolute)	–	–	–	s.c.
1	Bevacizumab	10 mg/kg	0.9% NaCl	100	90'*	i.v.



Repetition: Day 15

Number of cycles: Interferon alpha: max. 52 weeks or until disease progression; Bevacizumab: until disease progression

Note:

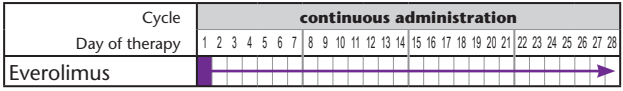
- (*) Bevacizumab: The initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.
- According to a retrospective analysis, the IFN dose had to be adjusted to 6 MIU (61% of patients) and to 3 MIU (31% of patients) without any loss of efficacy.

Literature:

Escudier B. et al., Lancet 370: 2103ff, 2007
Melichar B. et al., Ann Oncol 19: 1470ff, 2008

10.1.11 EVEROLIMUS *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Everolimus	10	–	–	–	p.o.



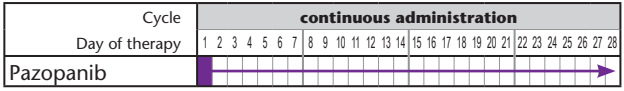
Repetition: * Continuous administration

Note:
- 10 mg at once (2 x 5 mg)

Literature:
Motzer R.J. et al., Lancet 372: 449ff, 2008

10.1.12 PAZOPANIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Pazopanib	800	–	–	–	p.o.



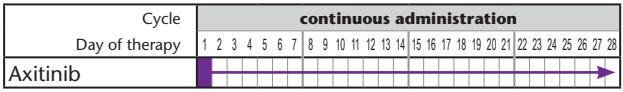
Repetition: * Continuous administration

Literature:

Sternberg C.N. et al., J Clin Oncol 28: 1061ff, 2010

10.1.13 AXITINIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Axitinib	10#	–	–	–	p.o.



Repetition: * Continuous administration

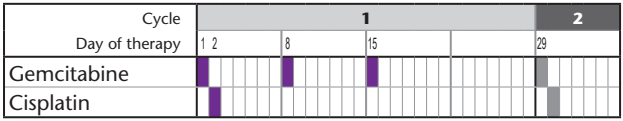
Note:
- (#) 10 mg devided into two equal doses, morning and evening

Literature:
Rini B. et al., Lancet 378: 1931ff, 2011

10.2 Urothelial Carcionoma

10.2.1 GEMCITABINE / CISPLATIN *XC592*

D	Drug	Do mg/m²	Di	V ml	T	R
1,8, 15	Gemcitabine	1000	0.9% NaCl	500	30'	i.v.
2	Cisplatin	70	0.9% NaCl	500	1h	i.v.



Repetition: Day 29

Number of cycles: 6

Note:
- Cisplatin (only if GFR ≥60 ml/ min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature:
von der Maase H., J Clin Oncol 18: 3068ff, 2000

10.2.2 VINFLUNINE *XC882*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Vinflunine	320	0.9% NaCl	100	20'	i.v.

Cycle	1			2
Day of therapy	1			22
Vinflunine				

Repetition: Day 22

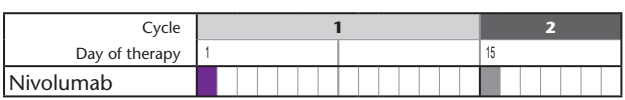
Number of cycles: 6

Note:
- *Caution:* Strict protection from light is required
- *Caution:* Thrombophlebitis; in case of peripheral access, Vinflunine should be followed by 250 ml 0.9% NaCl i.v.

Literature:
Krzakowski M. et al., J Clin Oncol 28: 2167ff, 2010

10.2.3 NIVOLUMAB *XA085*

D	Drug	Do mg/kg	Di	V ml	T	R
1	Nivolumab*	3	0.9% NaCl	100	1h	i.v.



Repetition: Day 15

Number of cycles: Until progressive disease or intolerability

Note:
- Nivolumab should be dissolved at 1-10 mg/ml
- (*) Nivolumab can also be administered at 240 mg flat-dose every 2 weeks (Zhao X. et al., Ann Oncol 28: 2002ff, 2017) or at 480 mg every 4 weeks (Long G.V. et al.; Ann Oncol 29: 2208ff, 2018)

Literature:
Sharma P. et al., Lancet Oncol 17: 1590ff, 2016
Sharma P. et al., Lancet Oncol 18: 312ff, 2017

10.2.4 PEMBROLIZUMAB *XA081*

D	Drug	Do mg	Di	V ml	T	R
1	Pembrolizumab	200	0.9% NaCl	100	30'	i.v.

Cycle	1			2
Day of therapy	1			22
Pembrolizumab				

Repetition: Day 22

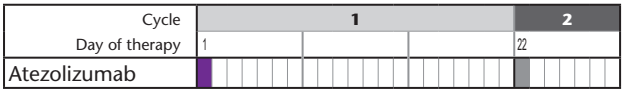
Number of cycles: Until progressive disease or intolerability

Note:
- Pembrolizumab should be dissolved at 1-10 mg/ml

Literature:
Bellmunt J. et al., N Engl J Med 376: 1015ff, 2017

10.2.5 ATEZOLIZUMAB *XA054*

D	Drug	Do mg	Di	V ml	T	R
1	Atezolizumab	1200	0.9% NaCl	500	30'*	i.v.



Repetition: Day 22

Number of cycles: Until progressive disease or intolerability

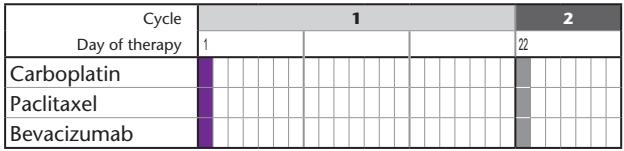
Note:
- (*) Atezolizumab: The initial dose should be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min
- Atezolizumab should be dissolved at 4.4 mg/ml

Literature:
Rosenberg J.E. et al., Lancet 387: 1909ff, 2016

10.3 Ovarian Cancer

10.3.1 CARBOPLATIN / PACLITAXEL + BEVACIZUMAB *XC772 + XA060*

D	Drug	Do	Di	V ml	T	R
1	Carboplatin	AUC 6	5% Glucose	500	30'	i.v.
1	Paclitaxel	175 mg/m²	0.9% NaCl	500	3h	i.v.
1	Bevacizumab	15 mg/kg	0.9% NaCl	100	90'*	i.v.



Repetition: Day 22

Number of cycles: 6

Note:

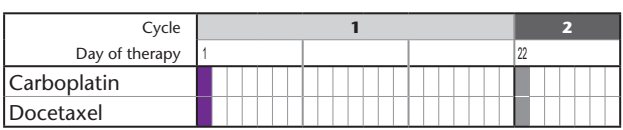
- Paclitaxel should be dissolved at 0.3 - 1.2 mg/ml
  Paclitaxel-accompanying medication:
  Dexamethasone 20 mg i.v. 30 min before Paclitaxel, or Dexamethasone 20 mg orally 6 h and 12 h before Paclitaxel. Additional premedication with 50 mg Ranitidine and 30 mg Diphenhydramine is recommended.
- Calculation of Carboplatin dose (Calvert):
  Dose (mg) = target AUC x (GFR + 25)

- Bevacizumab: start at cycle 2 through 22
- (*) Bevacizumab: The initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min.
  If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.
- Diluted Paclitaxel solutions should be administered through non PVC-containing administration sets.

Literature:
Burger et al., N Engl J Med 365: 2473ff, 2011

10.3.2 CARBOPLATIN / DOCETAXEL *XC184*

D	Drug	Do	Di	V ml	T	R
1	Carboplatin	AUC 5	5% Glucose	500	30'	i.v.
1	Docetaxel	75 mg/m²	0.9% NaCl	500	1h	i.v.



Repetition: Day 22

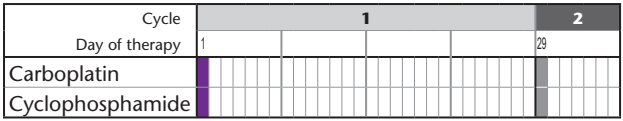
Number of cycles: 6

Note:
- Docetaxel should be dissolved at 0.3 - 0.74 mg/ml
- *Accompanying medication:*
  Dexamethasone 8 mg orally 2x daily for 3 days starting on day 1 before Docetaxel administration
- Calculation of Carboplatin dose (Calvert):
  Dose (mg) = target AUC x (GFR + 25)

Literature:
Vasey P.A. et al., J. Natl Cancer Inst 96: 1682ff, 2004

10.3.3 CARBOPLATIN / CYCLOPHOSPHAMIDE
XC180

D	Drug	Do mg/m²	Di	V ml	T	R
1	Carboplatin	300	5% Glucose	500	1h	i.v.
1	Cyclophosphamide	600	0.9% NaCl	500	1h	i.v.



Repetition: Day 29

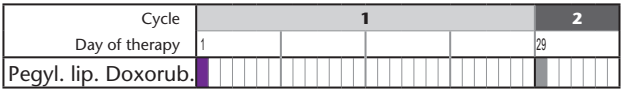
Number of cycles: 6

Note:
- *Mesna:* Dose is equal to 100% of the Cyclophosphamide dose, given as 20% of the Cyclophosphamide dose i.v. at hour 0, followed by 40% of the Cyclophosphamide dose given orally 2- and 6 hours after start of Cyclophosphamide

Literature:
Swenerton K. et al., J Clin Oncol 10: 718ff, 1992

10.3.4 PEGYLATED LIPOSOMAL DOXORUBICIN
XC452

D	Drug	Do mg/m²	Di	V ml	T	R
1	Pegylated liposomal Doxorubicin (Caelyx®)	50	5% Glucose	500	1h	i.v.



Repetition: Day 29

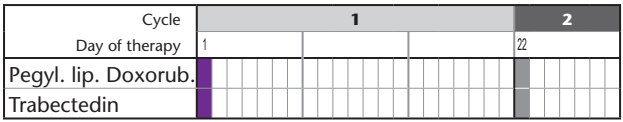
Number of cycles: 6

Note:
- Pegylated liposomal Doxorubicin should be dissolved in 250 ml of 5% Glucose if total dose is ≤ 90 mg and in 500 ml of 5% Glucose in case the total dose exceeds 90 mg.

Literature:
Gordon A., J Clin Oncol 19: 3312ff, 2001

10.3.5 TRABECTEDIN / PEGYLATED LIPOSOMAL DOXORUBICIN *XC454*

D	Drug	Do mg/m²	Di	V ml	T	R
1	Pegylated liposomal Doxorubicin (Caelyx®)	30	5% Glucose	500	1h	i.v.
1	Trabectedin	1.1	0.9% NaCl	1000	3h	i.v.



Repetition: Day 22

Number of cycles: 6

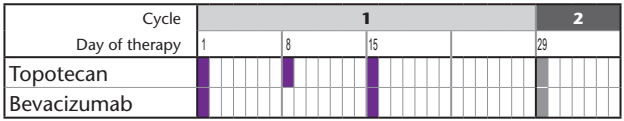
Note:
- Pegylated liposomal Doxorubicin should be dissolved in 250 ml of 5% Glucose if total dose is ≤ 90 mg and in 500 ml of 5% Glucose in case the total dose exceeds 90 mg.
- In the presence of a central venous device, Trabectedin can also be dissolved in 500ml 0.9% NaCl and be administered over 3h

Literature:
Kaye S.B. et al., Ann Oncol 22: 49ff, 2011

10.3.6 TOPOTECAN / BEVACIZUMAB

XC836 + XA060

D	Drug	Do	Di	V ml	T	R
1,8, 15	Topotecan	4 mg/m²	0.9 NaCl	50	30'	i.v.
1,15	Bevacizumab	10 mg/kg	0.9 NaCl	100	90'*	i.v.



Repetition: Day 29

Number of cycles: Until progressive disease or intolerability

Note:

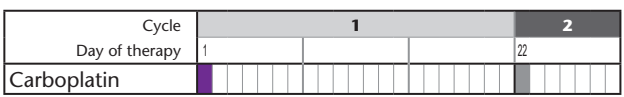
- Topotecan should be dissolved at 0.025-0.05 mg/ml
- (*) Bevacizumab: the initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.
- Instead of Topotecan, one can either use Paclitaxel 80 mg/m² d1,8,15,22 (q29) or pegylated liposomal Doxorubicin 40 mg/m² d1 (q29).

Literature:

Pujade-Lauraine E. et al., J Clin Oncol 32: 1302ff, 2014

10.3.7 CARBOPLATIN *XC172*

D	Drug	Do	Di	V ml	T	R
1	Carboplatin	AUC 5	5% Glucose	500	1h	i.v.



Repetition: Day 22

Number of cycles: 6

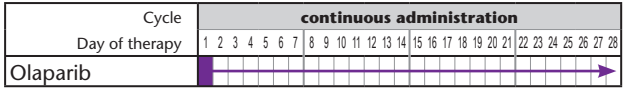
Note:
- Calculation of Carboplatin dose (Calvert):
  Dose (mg) = target AUC x (GFR + 25)

Literature:

The International Collaborative Ovarian Neoplasm (ICON) Group, Lancet 360: 505ff, 2002

10.3.8 OLAPARIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Olaparib	800	–	–	–	p.o.



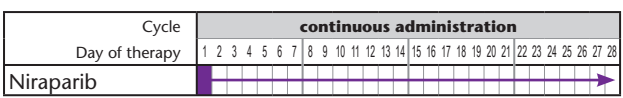
Repetition: * Continuous administration

Note:
- The recommended dose is 400 mg (eight capsules) taken twice daily

Literature:
Friedlander M. et al., Br J Cancer 119: 1075ff, 2018
Moore K.N. et at., N Engl J Med 379: 2495ff, 2018

10.3.9 NIRAPARIB *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Niraparib	300	–	–	–	p.o.



Repetition: * Continuous administration

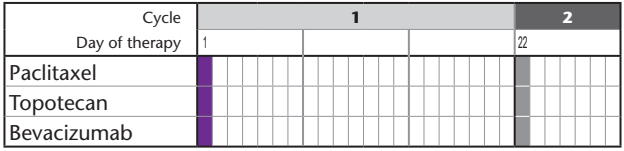
Literature:

Mirza M.R. et al., N Engl J Med 375: 2154ff, 2016

10.4 Cervical Cancer

10.4.1 PACLITAXEL / CISPLATIN / BEVACIZUMAB *XA060 + XC772*

D	Drug	Do	Di	V ml	T	R
1	Paclitaxel	135 mg/m²	0.9 NaCl	500	3h	i.v.
1	Cisplatin#	50 mg/m²	0.9 NaCl	500	1h	i.v.
1	Bevacizumab	15 mg/kg	0.9 NaCl	100	90'*	i.v.



Repetition: Day 22

Number of cycles: 6
optional: Bevacizumab can be continued until progressive disease or intolerability

Note:
- Paclitaxel should be dissolved at 0,3-1,2 mg/ml
- *Paclitaxel-accompanying medication:*
  Dexamethasone 20 mg i.v. 30 min before Paclitaxel, or Dexamethasone 20 mg orally 6 h and 12 h before Paclitaxel. Additional premedication with 40 mg Famotidine and 30 mg Diphenhydramine is recommended.

- (#) Cisplatin (only if GFR ≥60 ml/ min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl
- (*) Bevacizumab: The initial dose should be administered over 90 min. If the first infusion is well tolerated, the second infusion may be administered over 60 min.
  If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 min.

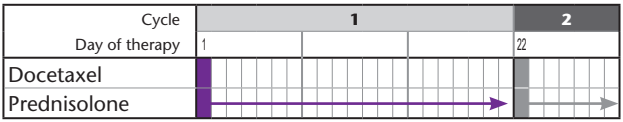
Literature:

Tewari K.S. et al., N Engl J Med 370: 734ff, 2014

10.5 Prostate Cancer

10.5.1 DOCETAXEL / PREDNISOLONE *XC412*

D	Drug	Do	Di	V ml	T	R
1	Docetaxel	75 mg/m²	0.9% NaCl	250	1h	i.v.
1-*	Prednisolone	10 mg	–	–	–	p.o.



Repetition: Day 22
* Continuous administratio

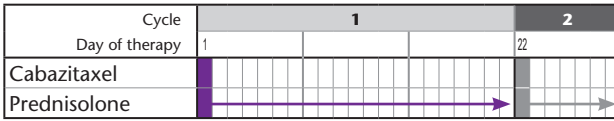
Number of cycles: 6

Note:
- Docetaxel should be dissolved at 0.3 - 0.74 mg/ml
- *Accompanying medication:*
  Dexamethasone 4 mg orally 12h, 6h, 1h before and 12h, 24h, 36h after Docetaxel administration. If there are no hypersensitivity reactions, Dexamethasone dose can be reduced to 2x 4 mg orally on the Day of Docetaxel administration.

Literature:
Tannock I.F. et al., N Engl J Med 351: 1501ff, 2004

10.5.2 CABAZITAXEL / PREDNISOLONE *XC166*

D	Drug	Do	Di	V ml	T	R
1	Cabazitaxel	25 mg/m²	0.9% NaCl	500	1h	i.v.
1-*	Prednisolone	10 mg	–	–	–	p.o.



Repetition: Day 22, * Continuous administration

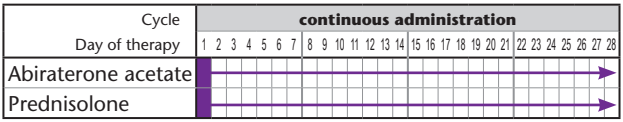
Number of cycles: 6

Note:
- Cabazitaxel should be dissolved at 0.1 - 0.26 mg/ml
- *Accompanying medication:*
  Dexamethasone 8 mg, Ranitidine 50 mg and Diphenhydramine 30 mg prior to Cabazitaxel is recommended.
- Diluted Cabazitaxel solutions should be administered through non PVC-containing administration sets.

Literature:
De Bono J.S. et al., Lancet 376: 1147ff, 2010

10.5.3 ABIRATERONE ACETATE / PREDNISOLONE *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Abiraterone acetate	1000	–	–	–	p.o.
1-*	Prednisolone	10	–	–	–	p.o.



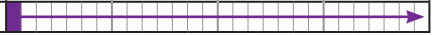
Repetition: * Continuous administration

Note:
- Abiraterone acetate: 1000 mg at once (4 x 250 mg)
- In the 1st-line setting in combination with androgen deprivation therapy

Literature:
De Bono J.S. et al., N Engl J Med 364: 1995ff, 2011
Ryan C.J., N Engl J Med 368: 138, 2013
James N.D. et al., N Engl J Med 377: 338, 2017

10.5.4 ENZALUTAMIDE *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Enzalutamide	160	–	–	–	p.o.

Cycle	continuous administration
Day of therapy	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
Enzalutamide	

Repetition: * Continuous administration

Note:

- Enzalutamide (four 40 mg capsules) administered orally once daily

Literature:

Scher H. et al., N Engl J Med 367: 1187ff, 2012

10.5.5 APALUTAMIDE *XA149*

D	Drug	Do mg	Di	V ml	T	R
1-*	Apalutamide	240	–	–	–	p.o.

Cycle	continuous administration
Day of therapy	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
Apalutamide	

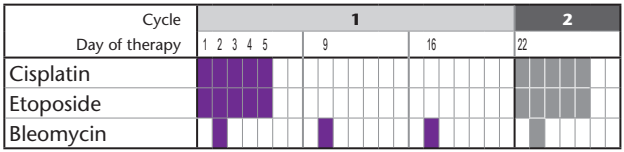
Repetition: * Continuous administration

Literature:
Chi K.N. et al., N Engl J Med 381: 13ff, 2019

10.6 Testicular Cancer

10.6.1 PEB *(Day 1-5: XC788; Day 8,15: XA149)*

D	Drug	Do	Di	V ml	T	R
1-5	Cisplatin	20 mg/m²	0.9% NaCl	500	30'	i.v.
1-5	Etoposide	100 mg/m²	0.9% NaCl	500	1h	i.v.
2,9, 16	Bleomycin	30 mg (absolute)	–	–	Bolus	i.v.



Repetition: Day 22

Number of cycles: 3-4

Note:

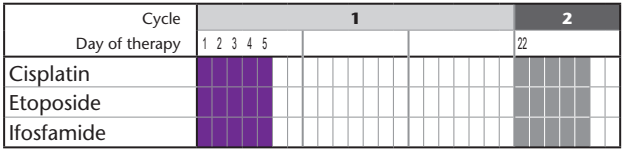
- Etoposide should be dissolved in 1000 ml 0.9% NaCl if total dose is ≥ 200 mg.
- Cisplatin (only if GFR ≥60 ml/ min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature:

Williams S.D. et al., N Engl J Med 316: 1435ff, 1987

10.6.2 PEI *XC796*

D	Drug	Do mg/m²	Di	V ml	T	R
1-5	Cisplatin	20	0.9% NaCl	500	30'	i.v.
1-5	Etoposide	75	0.9% NaCl	1000	1h	i.v.
1-5	Ifosfamide	1200	0.9% NaCl	500	1h	i.v.



Repetition: Day 22

Note:
- *Mesna:* Dose is equal to 100% of the Ifosfamide dose, given as 20% of the Ifosfamide dose i.v. at hour 0, followed by 40% of the Ifosfamide dose given orally 2- and 6 hours after start of Ifosfamide
- Increased risk of CNS toxicity if albumin ≤3.5 g/dl
- Cisplatin (only if GFR ≥60 ml/ min):
  Accompanying medication:
  Premedication: 500 ml 0.9% NaCl + 10 mEq KCl + 8 mEq $MgSO_4$ i.v. over 60 min.
  200 ml Mannite 20% over 30 min
  Postmedication: 500 ml 0.9% NaCl i.v. + 10 mEq KCl

Literature:
Harstrick A. et al., J Clin Oncol 9: 1549ff, 1991